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THE BRITISH JOURNAL

OF

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JUNE, 1948

COMMUNICATIONS

OX VITREOUS HUMOUR. 1.—THE RESIDUAL PROTEIN*

BY

A. PIRIE, G. SCHMIDT *and* J. W. WATERS

NUFFIELD LABORATORY OF OPHTHALMOLOGY AND DEPARTMENT OF CRYSTALLOGRAPHY, OXFORD

WHEN a vitreous humour is removed intact from an eye and put on a filter or hung from a clamp, a viscous fluid drips out of it until finally all that remains is a thin membranous wisp of material. Robertson and Duke-Elder (1933) describe the vitreous humour as " a gel composed of a meshwork of elastic fibrillae suspended in a viscous fluid," and we may suppose that the membranous stuff left after filtration forms the elastic fibrils of the intact vitreous body. This insoluble residue was first studied by Young (1894) and Mörner (1894), who considered that it was collagen because it dissolved in boiling water and the solution set to a gel on cooling. Mörner (l.c.) termed it the residual protein, and it has since been

* Received for publication, March 24, 1948.

known by this name. Duke-Elder (1930) described it as like gelatin, but Meyer (1945) classified it as an insoluble mucoid of unknown composition. The analyses of the insoluble residue show that it is a protein. Krause (1934) found 14·16 per cent. N and gave analytical figures for arginine, histidine, lysine, cystine, tryosine and tryptophane, all of which were present in the material analysed.

The experiments described in this paper bring forward further evidence in support of the view that the residual protein of vitreous humour contains a protein like collagen and describe the liquefying effect of preparations containing the enzyme collagenase on the vitreous body. These results are considered in relation to the well known acid and alkaline shrinkage of the vitreous humour, and are used to formulate a theory of the way in which the residual protein is laid down.

It is difficult to collect sufficient of the insoluble residue from the vitreous humour to identify it by analysis of the constituent amino-acids. One ox vitreous humour with a volume between 12-15 ml. yields only 2-3 mg. of insoluble residue. We have, therefore, attempted to identify this residue through its general properties, by amino-acid chromatography of hydrolysed material, by X-ray analysis and by enzyme analysis. The material appears to be fairly uniform, judged by solubility tests and enzyme digestibility, but we realise that the results we have obtained do not in any way prove that the insoluble residue of the vitreous humour consists of a single substance.

METHODS

Material. The experiments have been done using ox vitreous humours obtained within ½-2 hours after death of the animal. The humours were removed from the eye by making a complete equatorial cut through sclera, choroid and retina and allowing the vitreous humour to fall away from the retina, while still attached to the anterior half of the eye. It was then gently cut and pressed apart from the ciliary body and lens. The posterior lens capsule sometimes adheres to the vitreous humour, but can be removed with forceps.

Preparation of residual protein from vitreous humour. The insoluble residue may be separated from the soluble constituents by suspending the humour in saline and allowing the soluble substances to diffuse out into the surrounding fluid. Friedenwald and Stiehler (1935) found that the vitreous humour retained its form during prolonged washing in saline and that when it was finally filtered, the filtrate contained no organic material. We found that if an ox vitreous humour were left in the ice chest in saline

which was changed every few days, all detectable protein and hyaluronic acid had diffused out of the humour within 8-12 weeks. Such washed humours are more flaccid than when fresh and we have taken the insoluble residue remaining after their filtration as the residual protein. Salt may be removed from this by a few days' wash in distilled water.

The insoluble residue may also be prepared by filtration of the fresh vitreous humour followed by washing. This might seem the quicker method, but we found that very prolonged washing, by suspension in saline or water, was necessary to remove the small amount of soluble material remaining after the first filtration of the fresh humour.

Total nitrogen. Total nitrogen was estimated in 5-10 mg. samples frozen dried over P_2O_5. The samples were incinerated with 2 ml. H_2SO_4 + 0·5 g. catalyst (40 g. K_2SO_4, 10 g. $CuSO_4$, 0·17 g. SeO_2) incineration being continued for 5-8 hours after clearing. The ammonia was estimated by Markham's (1942) method.

Total carbohydrate. This was estimated by the orcin colorimetric method described by N. W. Pirie (1936).

Hexosamine. This was estimated by the method described by Elson and Morgan (1933).

Amino-acid chromatography. The method of Consden, Gordon and Martin (1944) was used.

GENERAL PROPERTIES OF INSOLUBLE RESIDUE

The residues from vitreous humour are grey and fibrous, showing considerable tensile strength and some anisotropy, particularly when stretched. When dried, each residue is a dark grey horny string. The colour seems to be due to adsorbed uveal pigment, cotton fibres and dust from the air and from the washing solutions. We found that the total nitrogen of such residues was near 12 per cent. and that they contained no hexosamine and from 3-7 per cent. total carbohydrate. Further purification of the residual protein while it was in this insoluble state was difficult owing to its capacity to adsorb other insoluble materials, such as cotton fibres, etc. From the general properties one may say that the vitreous residue appears to be made up largely of fibrous protein, but we felt that for further purification it was essential to get the protein, or proteins, into solution, even if this involved some degree of hydrolysis. We have, therefore, made a soluble preparation from the vitreous humour residues.

Preparation and properties of soluble protein from vitreous humour residues. Ox vitreous humours were washed as free as possible of soluble material by suspension in saline for long periods followed by filtration. The residues from about 50 humours were dissolved in 60 ml. HCl pH 1·8 on a boiling water bath. The cloudy solution was centrifuged and the small black sediment discarded. The supernatant was brought to pH 4 and the small flocculent precipitate that

came out was centrifuged off and has not been further investigated. It seems probable that this is an "artificial mucin," similar to those prepared by Meyer and Smyth (1937) and formed in this case from hyaluronic acid and any of the proteins present. The supernatant fluid from this precipitate was half saturated with ammonium sulphate by addition of an equal volume of saturated solution. An immediate copious precipitate came down. This was centrifuged out, re-dissolved in water and dialysed against distilled water in the ice chest. No further precipitate came out when the supernatant fluid from half saturation was wholly saturated with ammonium sulphate.

After several days' dialysis in the ice chest the solution of the precipitate got by 50 per cent. saturation with ammonium sulphate was frozen and dried. The preparation was a white fibrous material and had a total N 13·0-13·5 per cent. Further purification by dissolving in warm water, bringing the solution to pH 4, centrifuging and precipitation from the supernatant fluid by half saturation with ammonium sulphate gave a product that formed a firm jelly in the dialysis sac and had no ash, 14·8 per cent. N, no hexosamine and 6 per cent. total carbohydrate. We found that the vitreous humour residual protein lost 3·3 per cent. of its total nitrogen when taken into solution in dilute HCl. This loss probably represents loss of the amide group of glutamine, as Thierfelder and v. Cramm (1919) have shown that glutamine peptides are unstable under such conditions. If we correct for the loss of N on solution in acid the total nitrogen of the soluble product from ox vitreous humour residual protein is then 15·3 per cent.

The characteristic insoluble proteins of the animal body are collagen, elastin and keratin, with reticulin as a rather nebulous substance of unknown composition. The method of preparation and the general properties of the soluble stuff from ox vitreous humour residue suggests that the original material is like collagen and that it dissolves to form gelatin. Solubility in dilute acid is a property of collagen and precipitability by half saturation with ammonium sulphate and ability to form a gel are properties of gelatin. Yet the final value of 15·3 per cent. N is low for typical collagen or for gelatin. Bergmann and Stein (1939) found that collagen from ox Achilles tendon had 18·6 per cent. N. Few collagens have been analysed, other than those from skin and tendon; Mörner (1894) gave N 17·03 per cent. for ox cornea collagen and we have found that collagen prepared from ox cornea by the method of Bergmann and Stein (l.c.) had N 16·1 per cent. uncorrected for ash.

Both histologists and chemists accept cornea collagen as a typical collagen, so we felt that it would be valuable to compare it in some detail with the vitreous humour material. We have, therefore, prepared a soluble gelatin from ox cornea collagen and have compared its general properties with those of the soluble material from vitreous humour. We have also compared the amino-acid chromatograms of ox cornea gelatin and vitreous humour residues with that of commercial gelatin.

We found that we could prepare a soluble protein from ox cornea collagen by the same method as we had used with vitreous humour residue. This had no ash or hexosamine, total N 15·5 per cent. and 6 per cent. total carbohydrate, and in appearance and

properties was similar to the preparation from vitreous humour. If we correct the total N for the nitrogen lost on solution in dilute acid, the final figure is 16·0 per cent. total N.

AMINO-ACID CHROMATOGRAM OF OX VITREOUS HUMOUR RESIDUE AND OF CORNEA GELATIN COMPARED WITH COMMERCIAL GELATIN

Collagen and gelatin have a characteristic amino-acid composition. Bergmann and Stein (l.c.) found that ox Achilles tendon collagen contains 26·2 per cent. glycine and 17·1 per cent. proline and Schneider (1940) found 10·8 per cent. hydroxyproline in cow-hide collagen. No other protein so far analysed has such a high simultaneous concentration of these three amino-acids, so that a qualitative analysis, such as is given by an amino-acid chromatogram, may be used to help identify a protein suspected of being related to collagen or gelatin.

The method of partition chromatography on filter paper as a qualitative method of protein analysis was introduced by Consden, Gordon and Martin (1944). The principle is that if a drop of a solution of mixed amino-acids is put on a strip of filter paper and a water saturated solvent is then allowed to flow through the paper by capillary action, the amino-acids will be carried down the paper at different rates, depending on their solubilities in the two phases; water saturated with solvent and solvent saturated with water. They will thus be separated one from another. The presence of the separated amino-acids on the paper can be detected by the usual colour reaction with ninhydrin. A mixture of known amino-acids may be used as a marker solution. Each mixture will give a characteristic pattern of spots which ideally will be separated from one another on the filter paper and one can, therefore, compare one protein hydrolysate qualitatively with another by this technique.

The soluble preparations from ox vitreous humour and cornea were compared with a commercial gelatin (total N 17·0 per cent.) and with a mixture of glycine, proline and hydroxyproline made up in the proportions in which they occur in collagen. Three to five mg. of each preparation was dissolved in 1·0 ml. 6 *N* HCl and hydrolysed in sealed tubes at 110° overnight. The solutions were then dried *in vacuo* over H_2SO_4 and NaOH and all remaining HCl was removed by dissolving the residues again in 1 ml. H_2O and re-drying *in vacuo*, as before. This was repeated 5-6 times, to be certain of removing all acid.

When partition chromatograms are run on mixtures of amino-acids, the pattern which results when the paper is sprayed with ninhydrin and then heated is characterised by the following features :—

1. The presence of spots at different positions along the length of the run. The exact position of each spot depends upon the nature of the amino-acid component (Consden, Gordon and Martin (l.c.)), and to a certain extent also upon the amount of amino-acid contained in it (Fisher, Parsons and Morrison, 1948).

2. Each spot is coloured. Most amino-acids give spots with ninhydrin which are coloured rose or pink; some, *e.g.*, alanine, are rather more blue, while proline and hydroxyproline are instantly recognised by a characteristic yellow colour.

3. The size of each coloured spot varies. It has been shown that there exists a relatively simple relationship between the area of a spot and the amount of amino-acid in it (Fisher, Parsons and Morrison (l.c.)).

One dimensional partition chromatograms were run on solutions of the hydrolysates prepared as described above from ox vitreous humour and cornea, from commercial gelatin and on a marker solution of a mixture of glycine, proline and hydroxyproline made up in the proportions in which these amino-acids occur in collagen. The dilutions were so made that the volume of each hydrolysate put on the paper was 3 μl and contained 30 μg total N. Chromatograms of the three hydrolysates and of the mixture of amino-acids were run on the same sheet so that the pattern would not be affected by such adventitious sources of variation as those due to temperature changes and length of run. The chromatograms were run in two different types of solvent, so that two different types of pattern could be obtained, since the positions of the amino-acids in a developed chromatogram relative to each other and to the solvent front depend upon the solvent used. We used either phenol with 0·7 per cent. NH_3 or a pyridine-amyl alcohol mixture (Edman, 1945).

When the chromatograms were developed very striking similarities in the pattern exhibited by the three hydrolysates were at once evident (Fig. 1). The components in all three mixtures were comparable not only in position but in shades of colour and in spot area. This was true for chromatograms developed in both types of solvent. No attempt was made to identify all the amino-acid components of the hydrolysates, *e.g.*, by running two dimensional runs or by running hydrolysates in parallel with various synthetic mixtures; it was, however, evident that all three hydrolysates contained roughly comparable amounts of proline, hydroxyproline, glycine, glutamic and aspartic acids, and alanine.

Using the one dimensional technique and dealing with complex mixtures of components it is not possible to say whether or not small amounts of other amino-acid residues are present in one of

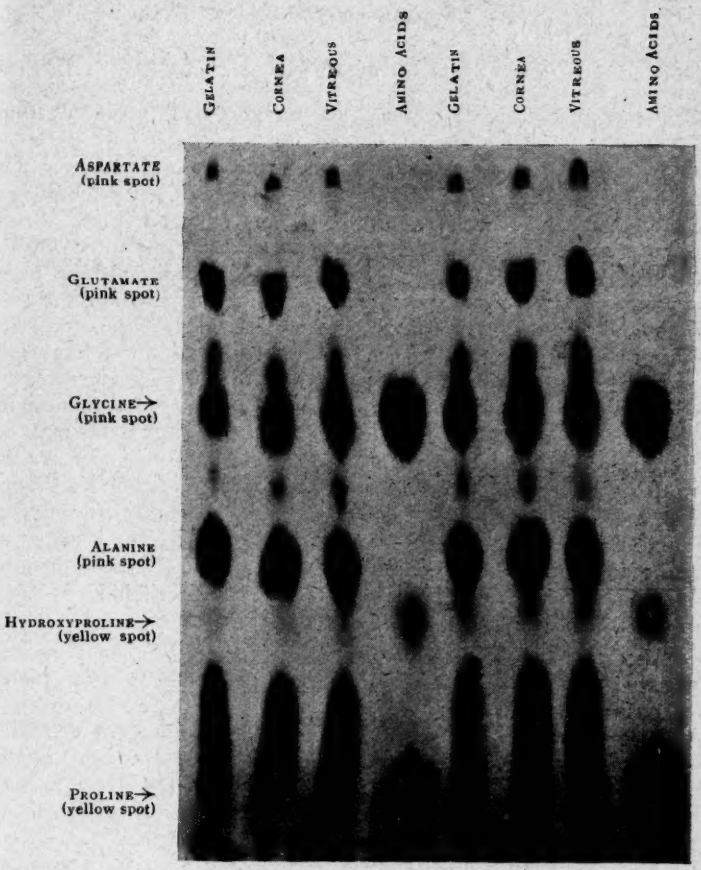

FIG. 1.

Partition chromatograms of hydrolysates of commercial gelatin, cornea gelatin, vitreous humour residual protein and a mixture of glycine, proline and hydroxy-proline. Whatman filter paper No. 1. Solvent saturated solution of phenol in water plus 0·7 per cent. NH_4OH.

the hydrolysates, but not in the others. While, therefore, there is no justification on the evidence of partition chromatography alone for identifying the nature and relative amounts of all the residues in the hydrolysates from the three sources, the evidence is sufficient to suggest that the vitreous humour protein might be a member of the collagen gelatin group.

X-RAY ANALYSIS OF RESIDUAL PROTEIN

We have taken X-ray photographs of vitreous humour residues, both in the unstretched and the stretched state. Material was prepared for X-ray analysis by combined washing and filtration. Vitreous humours were suspended in saline and left in the ice chest for several days with frequent changes of saline. This preliminary washing removed most of the soluble protein and some hyaluronic acid. The humours were next suspended and washed in successive changes of distilled water in order to remove most of the salt, which would interfere with the X-ray photograph of the protein. The humours were then filtered by suspension on a glass filter and, after a further wash, the residue on the filter was dried. This residue, collected from several vitreous humours, was photographed without being stretched. In a further experiment and in order to get some orientation of the material, the vitreous humours were only partly filtered after being washed and while still wet were bunched together with a loop of cotton and hung on a clamp to drip further. When nearly all the contained fluid had dripped out, a loop of cotton was tied round the lower end of the bunch of humours and a 50 g. weight was attached. The bunch was now hung in a dessicator and allowed to dry completely while under tension. This dried material was always deep grey or black, probably owing to the presence of uveal pigment.

About 20 mg. of dry material, as prepared above, were compressed into a round specimen and photographed on a flat plate at a specimen-to-film distance of 4·0 cm. with an X-ray beam capable of recording up to 60 A. A powder diagram was obtained whose spacings are recorded in Table I. The close resemblance of these spacings to the figures given by Astbury (1943) for collagen suggest that the protein of the vitreous humour can be classified as a collagen type.

Confirmation of this view has come from a study of stretched material prepared as already described. This method produced some degree of orientation, as was shown by the birefringence of the stretched residual protein which had been isotropic in the unstretched state. The X-ray photograph (Fig. 2), taken in this case on a cylindrical camera of radius 2·00 cm. and with the " fibre " axis of the specimen perpendicular to the X-ray beam, also demonstrates a considerable degree of orientation. The general agreement of the spacings of the X-ray reflections with those of oriented collagen fibres provides additional support for the view that the protein of the vitreous humour belongs to the collagen class.

TABLE I

SPACINGS GIVEN BY INSOLUBLE PROTEIN OF OX VITREOUS HUMOUR

Spacings obtained from unstretched specimen	*Spacings obtained from stretched specimen* (calculated from Fig. 1)	
	Equatorial	Meridian
A	A	A
2·9	2·1	2·9 (2·86; 2·91)
3·9	4·3 (4·4)	9·1 (9·5)
12·1	5·9 (5·62)	—
ca ·50	11·8 (10·9)	—

The figures in brackets are those given by Astbury (l.c.) for collagen.

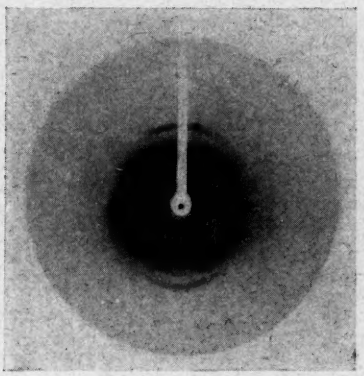

FIG. 2.

X-ray diagram of insoluble protein of ox vitreous humour. Stretched preparation showing orientation of fibres. Photograph taken with cylindrical camera, radius 3·00 cm. Cu radiation, Ni filtered.

ENZYME ANALYSIS OF VITREOUS RESIDUAL PROTEIN

The simplest test to find whether a given enzyme digests the residual protein of the vitreous humour is to see whether the enzyme takes the protein into solution. Previous workers have shown that the residual protein of the vitreous humour is, like collagen, dissolved by pepsin, but not by trypsin. We have confirmed this with our own preparations.

Through the kindness of Dr. W. E. van Heyningen we were able to test the effect of preparations of collagenase from *Cl. Welchii*. Bidwell and van Heyningen (1948) have shown that this enzyme digests only collagen and reticulin of all proteins so far tested, and this remarkable specificity makes it extremely useful for purposes of identification.

We found that a preparation of the enzyme readily dissolved the isolated residual protein of the vitreous humour. Small volumes of undiluted enzyme solution were next injected into the vitreous humour and Table II shows that collagenase preparations will liquefy the vitreous humour either in the eye or after extraction of the humour from the eye. Liquefaction was more complete after extraction, possibly because there was inevitable damage to the structure during removal from the eye, which made diffusion of the enzyme through the humour more rapid. After incubation with enzyme the vitreous humours were filtered and the residues on the filters—if any—were washed by suspension in water for some hours or days and were then dried *in vacuo* and weighed. In all experiments vitreous humours that had been injected with saline were used as controls.

TABLE II

EFFECT OF *Cl. Welchii* COLLAGENASE ON OX VITREOUS HUMOUR

Experiment No.	Vitreous preparation	Enzyme addition ml.	Saline addition ml.	Time at 37° hr.	Gross effect	Weight of residue mg.
1	in ox eye	0·4	—	16	½ liquid	1·4
	,,	—	0·4	,,	intact	3·4
2	in ox eye	0·2	—	24	½ liquid	1·7
	,,	—	0·4	,,	intact	3·6
3	freshly extracted	0·4	0·2	20	liquid	none
	,,	—	0·6	,,	intact	3·6
4	after six days in saline	0·4	—	22	liquid	none
	,,	—	0·4	,,	intact	—
5	residue protein fron filtered vitreous humour	0·1	0·9	24	dissolved	none

NOTE: *Cl. Welchii* collagenase preparation contained 220 Q enzyme units/ml. Eight ml. of enzyme preparation were mixed with 2 ml. antiserum containing 75 α units/ml., 70 θ units/ml. and 320 antihyaluronidase (Lister) units/ml. before use in these experiments.

The table shows that the collagenase preparation had an obvious liquefying effect on the vitreous humour and, in conjunction with this, the weight of insoluble residue remaining after filtration was smaller than in the controls. In some cases the residual protein was completely dissolved. The weights of the control residues were rather high, probably because they were only washed in water for a day or two before drying. We feared that prolonged washing would disintegrate the residues from the enzyme treated vitreous humours and so restricted the washing of all residues to short periods.

The evidence given by the various experimental methods described all suggests that the insoluble residue of the ox vitreous humour is largely made up of a protein of the collagen class. To the ophthalmologist, knowledge of the chemistry of the vitreous humour is mainly of interest if it increases knowledge of its development and of the normal and abnormal behaviour and appearance of the vitreous humour during life. The experiments reported here tell us nothing of the development of the vitreous humour, but we think that the results can be useful in formulating a more precise picture of the " meshwork of elastic fibrillae suspended in a viscous fluid," which Robertson and Duke-Elder (l.c.) considered to be the structure of the vitreous humour, as a result of their work on its physical properties. In the following paragraphs we have, therefore, attempted an interpretation of the chemical results in terms of the behaviour of the vitreous humour under various conditions and we report experiments which we believe support this interpretation.

COMPARISON OF VITREOUS HUMOUR WITH COLLAGEN GEL

The insoluble protein in the vitreous humour appears to be laid down in a state of extremely fine division, either as a very fine meshwork of fibres or as extremely thin sheets. Such a network of molecular fineness is on the borderline of what is usually considered to be the structure of a gel.

We have, therefore, compared the properties of the vitreous humour with the properties of a collagen gel. Soluble collagen was first described by Nageotte (1927), who prepared it by treating rat tail tendon with very dilute acetic acid. Most of the tendon goes into solution and collagen may be re-precipitated either as macroscopic fibres, by neutralising the solution, or as a firm gel by dialysing the solution against distilled water to remove salts and acid. Nageotte and Guyon (1931) found that rat tail tendon collagen is the only collagen that goes into solution in this way. Tendons from the ox are insoluble.

We have prepared collagen gels of varying concentration from filtered solutions of rat tail tendon and have compared these with the vitreous humour. Gels in which the concentration of collagen is 0·3 per cent. or over do not break down when put on a filter, but gels of 0·07 per cent. or lower concentrations, could be filtered in exactly the same way as the vitreous humour, the collagen being left behind on the filter as a wisp-like residue. This collagen residue showed considerable anisotropy, particularly when stretched, rather like the residue from the vitreous humour and it stained brown with silver, again like the vitreous humour residue.

There were, however, two important differences between the gel residue and the vitreous humour residue. In the first place, the vitreous humour residue showed considerable tensile strength, even when wet, while the gel residue showed little or none. A more important difference was that when the gel residue was suspended in water it swelled and finally went completely into solution, whereas the vitreous humour residue showed no sign of dissolving under such conditions and remained intact for many months.

We consider, therefore, that the structure of the vitreous humour is rather different from a collagen gel, the differences between them perhaps showing that there is a firmer, more stable arrangement in the vitreous humour, which may perhaps be considered as a network of submicroscopic fibres. This picture, if correct, must conform with what is known of the properties of collagen and collagen fibres obtained from other sources.

SWELLING OF COLLAGEN AND SHRINKAGE OF VITREOUS HUMOUR

One of the most characteristic properties of collagen is its capacity to swell, the degree of swelling varying with the acidity or alkalinity of the solution. Fig. 3 gives the swelling curve of fresh, undried ox cornea collagen (Pirie, 1947) and shows that there is maximal swelling in acid, minimal at neutrality and intermediate swelling in alkaline solutions. Highberger (1939) has found that the isoelectric point of native skin collagen is pH 7·4-7·6, which corresponds with the zone of minimal swelling of cornea collagen.

If we apply these results to the vitreous humour we see that the fibres in it will be *minimally* swollen under normal conditions of neutrality, but will swell with any change, either towards acidity or alkalinity. This is exactly the reverse of the effect of acidity or alkalinity on the size of the vitreous humour as a whole. Many investigators have shown that there is very marked shrinkage of the vitreous humour in either acid or alkali and we found that the same is true for vitreous humour residues washed free from the

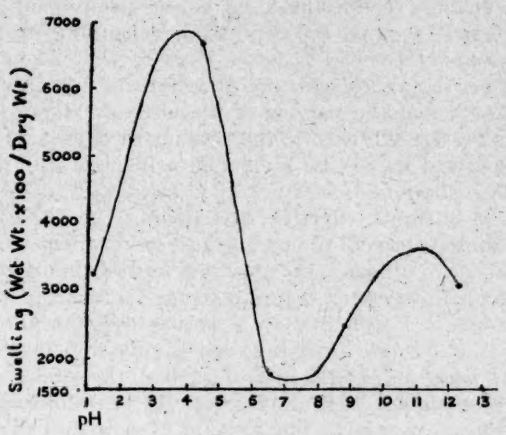

FIG. 3.

Swelling curve of ox cornea collagen.

soluble contents. A vitreous humour residue may have a wet weight of 10-15 g. at neutrality and one of 1-2 g. after suspension in $\frac{N}{100}$ HCl.

We think that shrinkage of the vitreous humour and of the isolated vitreous humour residues in acid and alkali may be explained on the assumption that the fibres in it are arranged in a network. Küntzel (1926) showed that collagen fibres from rat tail shortened in length as they swelled in acid, the shortening being directly proportional to the degree of swelling of the fibre. This was confirmed by Jordan-Lloyd and Marriott (1935). If we consider a loose network of collagen fibres, swelling of these fibres will cause a shortening of each individual one. If the nodes are fixed, the shortening of each fibre will cause an over-all contraction of the whole structure because the lateral swelling of the fibres simply fills up the interfibrillar spaces which originally are very large compared to the volume of the fibres.

We suggest that the shrinkage of the vitreous humour in acid or alkali is due to the swelling and shortening of the fibres within it. Some evidence in favour of this view may be got from a study of the effect of salts on the volume changes in acid and alkali of the vitreous humour and of the isolated residues. Loeb (1920) showed that acid swelling of gelatin was depressed by salts, the degree of depression at any particular pH and salt concentration depending

upon the valency of the anion. Alkaline swelling of gelatin was also depressed by salts, the depression depending on the valency of the cation.

If salts act in this way on the fibres of the vitreous humour we should expect that the volume of the vitreous humour, which we suggest is *inversely* related to the volume, or degree of swelling of the fibres within it, will be greater in acid plus salts than in acid alone. We should also expect that salts with di- or tri-valent anions will be more effective in reducing the shrinkage of the vitreous humour in acid than salts with monovalent anions.

A great deal of work on swelling and shrinkage of vitreous humour has already been done, in some of which the effect of salts was examined. A difficulty in assessing these results is that the fresh vitreous humour contains both soluble and insoluble constituents and when suspended in acid or alkali the soluble constituents —if not precipitated—will diffuse into the surrounding fluid, thus altering its composition. The amount of salts diffusing out of the humour may appreciably change the concentration in the solution unless the volume of solution is very great or it is renewed after some time.

EFFECT OF SALTS ON VOLUME OF WASHED VITREOUS HUMOUR RESIDUES

We have examined the effect of salts on acid and alkaline swelling of the washed vitreous humour residues. By using such washed residues we have avoided any complication due to precipitation of vitreous mucin by acid, and lack of equilibrium owing to outward diffusion of soluble constituents, including salts. The results we obtained were the same as those for fresh vitreous humours, but we found that the final volume was much more rapidly obtained and, in general, the valency effect was more clearly shown.

Each washed residue or fresh vitreous humour was put in a stoppered flask containing 200 ml. of the appropriate solution and left on the bench for 24-48 hours. The volume of the vitreous residue or fresh vitreous humour was determined both before and after suspension in fluid by placing in a measuring cylinder of appropriate size and reading off the volume. The pH of the solutions was determined electrometrically before and after immersion of the vitreous preparations in them.

Table III shows the percentage decrease in volume of washed vitreous residues after immersion in different salt solutions at either acid or alkaline pH. The first experiment shows that in acid the monovalent anion Cl^- has practically no effect on vitreous shrinkage, the divalent anion SO_4^{--} diminishes vitreous shrinkage considerably and the trivalent anion $Fe(CN)_6^{---}$ in a much lower concentration almost abolishes the shrinkage. Experiment two shows

TABLE III

EFFECT OF SALTS ON ACID AND ALKALINE SHRINKAGE OF WASHED VITREOUS HUMOUR RESIDUES

Expt.		HCl at pH 2·0			
	Salt added	None	$\frac{M}{128}$ NaCl	$\frac{M}{128}$ Na_2SO_4	$\frac{M}{1024}$ $K_3Fe(CN)_6$
1	Per cent. decrease in volume	82	79	36	14

		HCl at pH 1·8					
	Salt added	None	$\frac{M}{64}$ $CaCl_2$	$\frac{M}{64}$ $AlCl_3$	$\frac{M}{64}$ K_2SO_4	$\frac{M}{1024}$ K_2SO_4	$\frac{M}{1024}$ $K_3Fe(CN)_6$
2	Per cent. decrease in volume	94	92	92	50	85	30

		NaOH at pH 11·1		
	Salt added	None	$\frac{M}{512}$ NaCl	$\frac{M}{512}$ $CaCl_2$
3	Per cent. change in volume	−78	−63	+18

		NaOH at pH 11·4				
	Salt added	None	$\frac{M}{256}$ KCl	$\frac{M}{256}$ K_2SO_4	$\frac{M}{256}$ $CaCl_2$	$\frac{M}{32}$ K_2SO_4
4	Per cent. decrease in volume	61	77	56	23	36

that calcium chloride and aluminium chloride do not depress shrinkage in acid, which is in favour of the view that this effect in acid is dependent on the valency of the anion not the cation. It also shows that although $\frac{M}{64}$ K_2SO_4 depresses shrinkage, $\frac{M}{1024}$ has little effect, while $\frac{M}{1024}$ $K_3Fe(CN)_6$ a salt with a trivalent anion, has a greater effect than $\frac{M}{64}$ K_2SO_4. Experiments three and four show that in alkali $CaCl_2$ reduces shrinkage—in fact, in one case there is slight expansion—while KCl and NaCl have no effect. In

alkali, therefore, shrinkage is depressed according to the valency of the cation of the added salt.

We found that if those vitreous residues which had been immersed in $K_3Fe(CN)_6$ or K_2SO_4 solutions were washed free of salts and then put in HCl of pH2 they shrank further until they equalled in size the vitreous residues that had been placed directly in acid. This shows that the salts that depress vitreous shrinkage have no permanent effect. The dry weight of fully shrunken residues whose volume was between 1-2 ml. was the same as the dry weight of vitreous residues held at neutrality, showing that the shrinkage was not due to solution of the residue by the acid.

These experiments were repeated using fresh vitreous humours. We found that one ox vitreous humour could change the pH of 200 ml. dilute acid or alkali by as much as two units and it was necessary to transfer the humours to fresh solutions after 24 hours, both in order to obtain the required pH and also to dilute the salts which had diffused out of the vitreous itself.

TABLE IV

EFFECT OF SALTS ON ACID AND ALKALINE SHRINKAGE OF FRESH VITREOUS HUMOUR

		HCl at pH 2·2			
Expt.	Salt	None	$\frac{M}{128}$ NaCl	$\frac{M}{128}$ K_2SO_4	$\frac{M}{1024}$ $K_3F3(CN)_6$
1	per cent. decrease in volume	71	76	62	26

		NaOH at pH 11·2				
	Salt	None	$\frac{M}{256}$ KCl	$\frac{M}{256}$ $CaCl_2$	$\frac{M}{32}$ KCl	$\frac{M}{32}$ $CaCl_2$
2	per cent. decrease in volume	70	62	8	52	8

The shrinkage of fresh vitreous humour in acid or in alkali was also depressed by the addition of salts, in acid the depression was related to the valency of the anion and in alkali to the valency of the cation. Table V shows that $\frac{M}{4}$ KCl has about the same effect as $\frac{M}{32}$ K_2SO_4 or $\frac{M}{1024}$ $K_3Fe(CN)_6$.

Table V

EFFECT OF DIFFERENT CONCENTRATIONS OF KCl, K_2SO_4 AND $K_3Fe(CN)_6$ ON VOLUME OF FRESH VITREOUS HUMOUR IN HCl AT pH 1·8

Molarity of salt	Final volume of vitreous humour ml.		
	KCl	K_2SO_4	$K_3Fe(CN)_6$
0	1·5	1·5	1·5
M/4	8·0	—	—
M/32	5·0	8·0	—
M/64	—	5·0	—
M/128	2·5	2·5	—
M/512	3·5	3·0	—
M/1024	3·5	4·0	7·5

All vitreous humours had an initial volume of 14—15 ml. The final volumes were measured after 64 hours. The humours were transferred to fresh solutions after 24 hours, to avoid effect of salts diffusing from vitreous itself.

Salts, therefore, depress *shrinkage* of the vitreous humour, just as Loeb (l.c.) found they depressed *swelling* of gelatin. We think it is most likely that they are having the same effect in both cases, depressing the acid and alkaline swelling of a protein. The results support the view that the insoluble vitreous residual protein is laid down as a meshwork of fibres, each of which will swell and shorten in acid or alkali and so cause shrinkage of the whole vitreous humour.

Discussion

Slit-lamp examination of the vitreous humour during life or after extraction shows that it is not optically empty, but that it may contain sheets or membranes of reflecting material. Friedenwald

and Stiehler (1935), using the slit ultra-microscope to examine the extracted vitreous humour of the ox, observed fairly regular bright reflections which they interpreted as due to very thin sheets of the residual protein. The bright reflections ran roughly parallel to the surface of the vitreous humour and were separated from one another by spaces of 0·5-3 microns. Friedenwald and Stiehler considered that the thickness of the sheets was of the same order of magnitude as the wave length of light and they thought that cohesion between sheets might form the visible opacities of the degenerating humour. Vogt (1941), who has studied the vitreous humour in the living human eye, speaks of the scaffolding of the vitreous body and states that it is predominantly lamellar in structure, that is, membranous, but that a fibrillar structure in the membranes can often be made out. Vogt's very beautiful pictures of vitreous opacities fit with the idea that these are formed by cohesion between membranes or fibres.

The vitreous humour of the ox appears to be a more rigid structure than that of any other animal so far examined. Meyer, Smyth and Gallardo (1938) have found that ox vitreous humour contains a great deal more hexosamine than the humours of other animals. This indicates that the hyaluronic acid content of ox vitreous humour is greater and probably explains its greater rigidity. In spite of such quantitative differences between animals, there appears to be a qualitative similarity, both in the slit-lamp appearance and in the chemistry of the vitreous humours of different species.

If the experimental evidence given here is accepted the picture of the structure of the vitreous humour becomes more complex. It cannot be considered as uniform, but must be made up of at least two " structures," the collagen-like network and the hyaluronic acid and protein jelly. Liquefaction of the humour follows enzymic hydrolysis of the network and therefore one may say that this network is essential for maintenance of a normal vitreous humour. Yet it does not form the humour, being minimally swollen at neutrality and occupying only a very small part of the total volume. It seems to us that it is the relation of the network to the jelly which is of first importance and must be taken into account in any theories of the causes of vitreous swelling and vitreous degenerations.

SUMMARY

1. X-ray photography, amino acid chromatography and enzyme analysis provide evidence that the residual protein of the ox vitreous humour is largely a collagen type.

2. Enzyme preparations containing collagenase liquefy the ox vitreous humour.

3. The bearing of this result on the conception of vitreous humour structure is discussed.

We are deeply indebted to Dr. D. S. Parsons and Dr. R. B. Fisher for carrying out the amino-acid partition chromatograms on our material and for their interpretation of them. We also wish to thank Mr. Tugwell, photographer to the Radcliffe Infirmary, for the care he has taken in preparing the photographs of the chromatograms.

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VARIATION OF PUPIL SIZE WITH CHANGE IN THE ANGLE AT WHICH THE LIGHT STIMULUS STRIKES THE RETINA*

BY

K. H. SPRING *and* W. S. STILES

THE possibility of a variation in pupil size depending on the part of the natural pupil through which the light from the external field enters the eye has not been examined hitherto. Such a variation might occur for two reasons: (*a*) since the apparent brightness of an illuminated field is reduced if the rays enter near the edge rather than near the centre of the pupil (directional sensitivity of the retina†), a slightly larger pupil might be expected in the former case; (*b*) if, as is possible, the protective action of the constricted pupil consists not so much in reducing the total light flux as in excluding rays which would otherwise strike the retina obliquely, such rays might prove more effective in closing the pupil than rays incident normally. The pupil would then be smaller for rays entering near the edge. While variations from these causes are likely to be smaller than the effects of changes in field brightness and field area, they would be of considerable theoretical interest and would have a bearing on the efficient design and use of optical instruments. In the present work, carried out at the request of the Director of Scientific Research, Admiralty, measurements of the pupil were made under conditions specially arranged to reveal any change of size with change in the point of entry of the light in the pupil.

To obtain the greatest possible separation between rays entering centrally and near the edge, the pupil must be fully dilated. On the other hand it is the pupil of moderate size which is most sensitive to changes in the conditions of illumination. Both requirements were met by exposing the illuminated field to one eye only, the pupil of this eye being kept fully dilated with a mydriatic, and by determining by flash photography the variations in size of the free (unmydriasised) pupil of the other eye which was kept in the dark. It was confirmed that a given light stimulus entering either eye affected both pupils about equally and that mydriasis of one pupil did not interfere with the reaction of the other.

In the two sets of main measurements, made on 12 subjects, the

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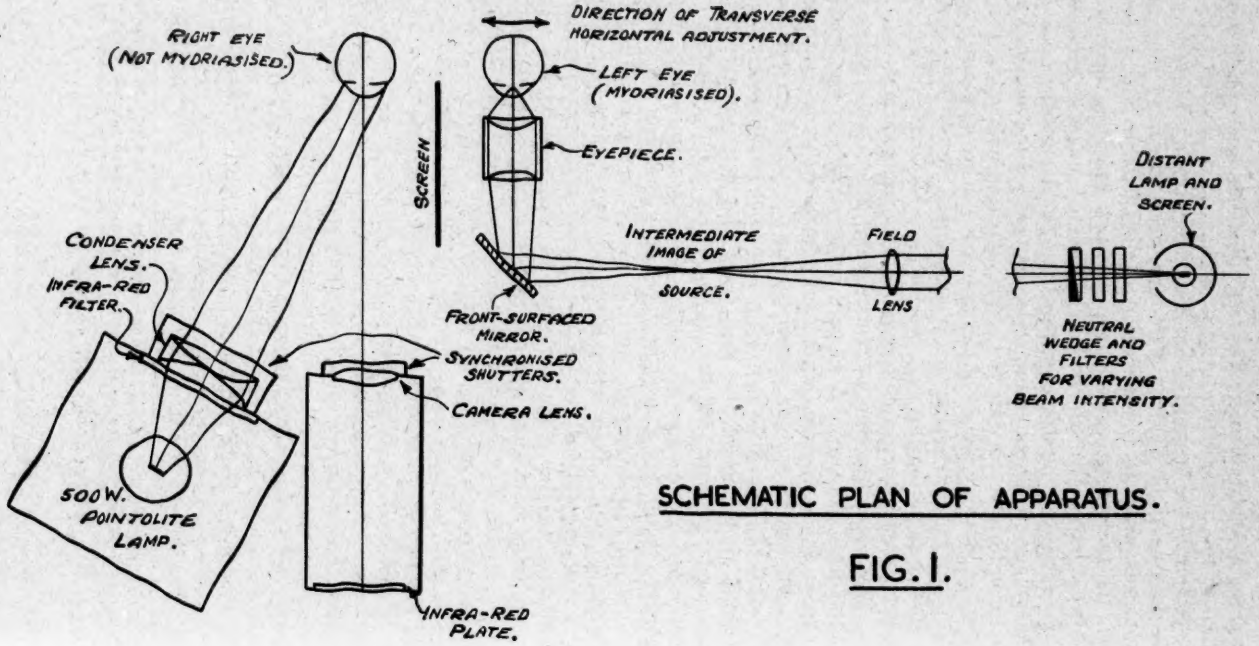
† For a review of the work done up to 1939 on this property of the retina (Stiles-Crawford effect) see Stiles, *Science Progress*, Vol. XXXIII, p. 176, 1939.

rays from a Maxwellian field of 52° diameter (white light) were focused in the plane of the mydriasised pupil of the left eye, the cross-section of the beam in this plane being approximately 0·5 mm. Thus the free right pupil was the one photographed. The principle of the apparatus is made clear by the sketch in Fig. 1 (not to scale). The subject's head was kept rigid by requiring him to bite on a dental impression which was clamped to a massive lathe slide-rest mounted on the table carrying the optical apparatus. The 3-dimensional adjustment of the slide-rest enabled the subject's eyes to be brought into precisely the correct position with respect to the apparatus. Also by means of the transverse horizontal adjustment the head could be moved so that the rays from the 52° field entered the dilated pupil of the left eye at any point on a horizontal diameter. For photographing the right pupil, the infra-red light from a 500 watt Pointolite was focused on the eye and exposed by a shutter for 1/20th sec. A second, synchronised shutter exposed the camera lens. Kodak Extra-Rapid Infra-red plates were used.

In the first series of main measurements the beam entered the left eye centrally. The variation of the apparent pupil size (apparent horizontal diameter) of the right eye was determined for field intensities from zero to 10^5 luxons (photons)*. The results for the 12 subjects (average age 29, range 25-46) are shown in Fig. 2, each curve being based on 2 or 3 sets of measurements. In each set, the observations began after the subject had been in the dark for about 15 min. Thereafter, the right pupil was photographed after 3 min. exposure of the left eye to each of an increasing series of field brightnesses. The left pupil was not mydriasised. There are very large individual differences and it may be noted that for several subjects the decrease in pupil size with increase in field brightness appears to occur in two stages. The results of these subjects are chiefly responsible for the slight irregularity in the mean curve (Fig. 3) at an intensity in the neighbourhood of $10^{0.5}$ luxons (marked X). The second curve in Fig. 3 gives the mean results obtained in an unpublished investigation by the Admiralty Research Laboratory in which the subjects (52, average age 24) viewed, binocularly and with the natural pupil, a field of 50° diameter. This curve also shows a slight irregularity (marked Y) but at a much lower intensity, $10^{-0.9}$ luxons.

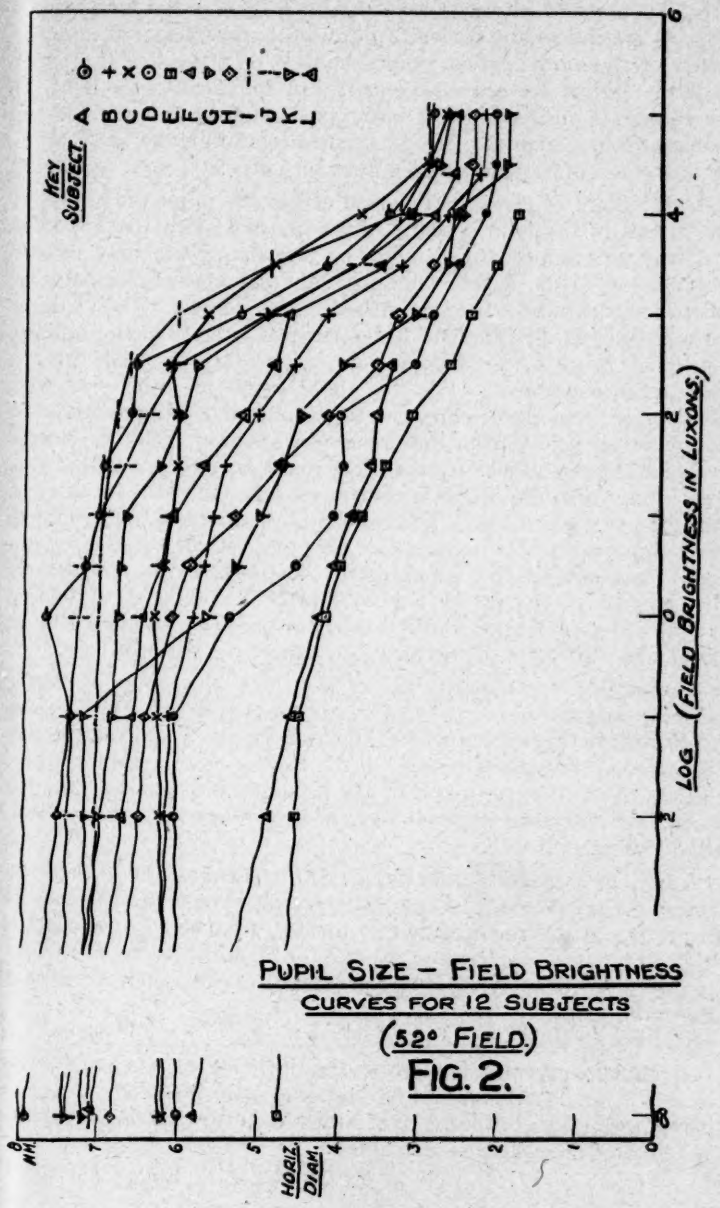
To investigate the variation of apparent pupil size with point of entry a fixed field brightness in the range indicated in Fig. 3 was used. The left pupil was mydriasised, and the right photographed

* The photon is a unit of retinal illumination, and is the illumination corresponding to an external field of brightness one candle per square metre seen through a pupil of 1 sq. mm. area. Following Blottiau, the term "luxon" is now used to avoid confusion with the "photon" of quantum theory.



SCHEMATIC PLAN OF APPARATUS.

FIG. 1.



PUPIL SIZE – FIELD BRIGHTNESS
CURVES FOR 12 SUBJECTS
(52° FIELD.)

FIG. 2.

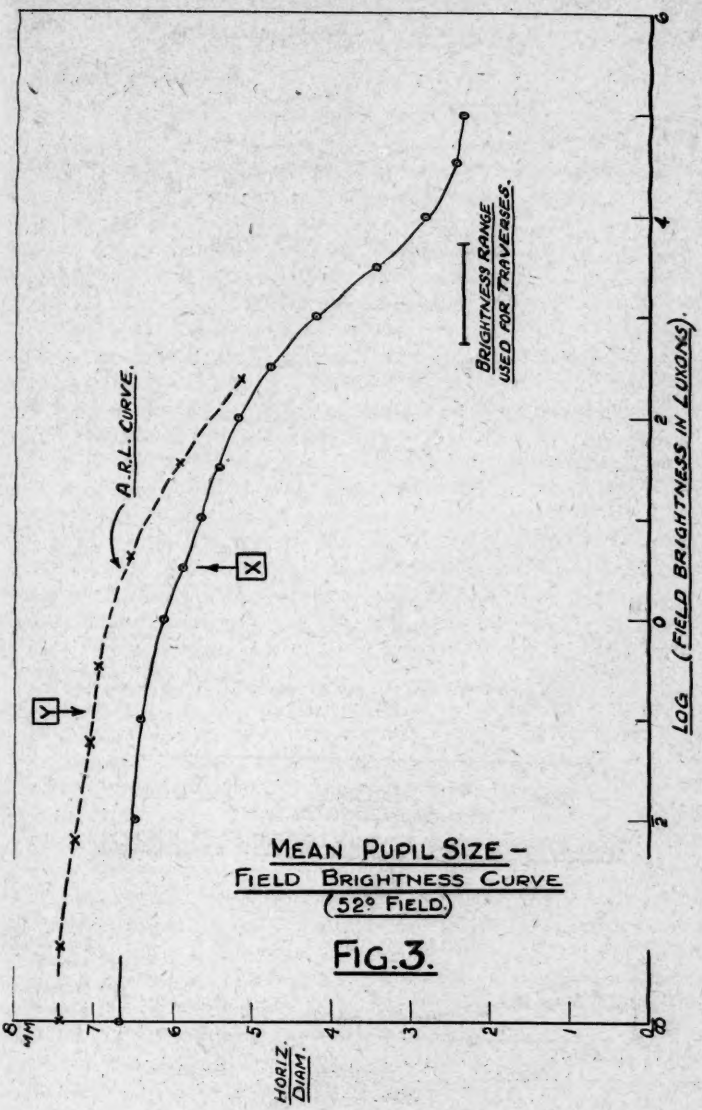
after the usual 3 minute preadaptation. The individual results (Fig. 4) are the means derived from 3 or 4 traverses of the pupil. A few of the more regular graphs show a tendency for the pupil to dilate slightly for eccentric entry. For the mean curve (Fig. 5) the change is very small and may not be significant: there is an increase from a diameter of 3·75 mm. for central entry to 4·1 mm. for entry at 3 mm. nasal and 4·0 mm. for entry at 3 mm. temporal.

As the point of entry is traversed across the pupil the apparent brightness of the field changes. For foveal vision, the apparent brightness is reduced by a factor η, given approximately by the formula $\log \eta = -0{\cdot}05d^2$ where d is the distance of the point of entry from the pupil centre, expressed in mm. (Stiles, 1939). Taking for each subject the gradient of the curve of pupil diameter against log (field brightness) (Fig. 2), at the brightness used for the traverse measurements (Fig. 4), the change of pupil size with position of the point of entry can be calculated, on the assumption that it arises solely from the change in apparent field brightness predicted by the above formula. The mean curve calculated in this way is shown in Fig. 5. It is evident that the observed variation is less than that calculated. The calculation assumes in effect that at the brightness levels in question only the retinal cones are concerned in determining the pupil size. The retinal rods have nearly the same sensitivity for all points of entry of a light stimulus and if they are participating in the control of the pupil the variation of pupil size with point of entry may be expected to be less.

Comparison for each subject of the pupil size obtained in the traverse measurements (Fig. 4) with the pupil size at the same brightness in the brightness level measurements (Fig. 2) shows that the mydriasis of the left pupil in the former case has not affected the control of the right pupil by the light stimulus entering the left eye. The difference in pupil size for the two cases averaged over the 12 subjects is 0·13 mm.

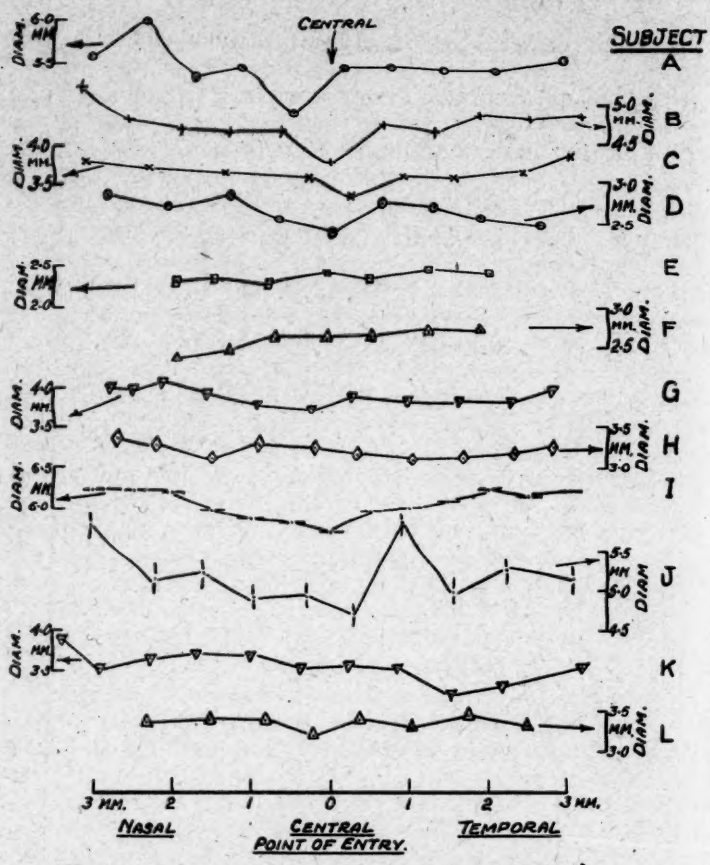
It may be concluded from the present measurements (*a*) that rays entering near the edge of the dilated pupil, and hence incident on the retina at an angle with the normal, produce no abnormally high pupillomotor effect and (*b*) that for practical purposes the part of the pupil through which light enters the eye is not a factor in determining pupil size.

Acknowledgment. The work described above was carried out in the Light Division of the National Physical Laboratory on behalf of the Chief of the Royal Naval Scientific Service, by whose permission this paper is published.



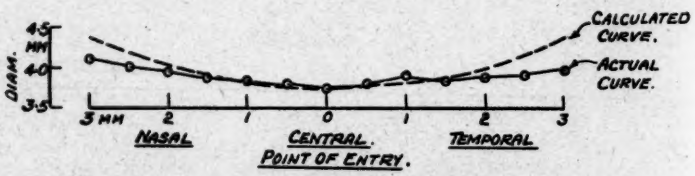
MEAN PUPIL SIZE – FIELD BRIGHTNESS CURVE (52° FIELD)

FIG. 3.



TRAVERSES FOR 12 SUBJECTS (52° FIELD.)

FIG. 4.



CALCULATED, AND MEAN EXPERIMENTAL, CURVES.

FIG. 5.

APPARENT SHAPE AND SIZE OF THE PUPIL VIEWED OBLIQUELY*

BY

K. H. SPRING *and* W. S. STILES

IN studies of the response of the peripheral retina, a knowledge of the apparent shape and size of the pupil for large angles of view is sometimes necessary. By photographing the pupil at various angles in the horizontal meridian from 20° nasal to 105° temporal the mean results shown in Table I were obtained for a group of 13 subjects. In the case of the large pupil, the pupil was fully dilated with a mydriatic and the field of view was kept dark until the light-flash for the exposure was given. These results refer therefore to a pupil whose actual size may be taken as constant for all angles of view. The variations of apparent size are attributable solely to the obliquity and to the refraction of the cornea and aqueous. For the small pupil results on the other hand the pupil was free, *i.e.*, no miotic was used, but it was kept small by being permanently exposed to the light source used for the photography. In these circumstances the actual pupil size could not be taken as constant for the various exposures and, for this reason, only the ratio of horizontal and vertical diameters determining the approximate shape of the apparent pupil is reported. The individual variations in shape for both large and small pupils are shown by the plots of this ratio in Figs. 1 and 2.

In view of the angular displacement of the optic axis relative to the visual axis, the mean curves of Figs. 1 and 2 may be expected to be symmetrical about an ordinate at about 5° temporal. As far as can be judged with only one observational angle on the nasal side, this is the case. It will be noted (column 3 of Table I) that for the large pupil the apparent vertical diameter varies little with angle but shows a maximum at about 80° temporal.

For a simplified eye consisting of a refracting sphere of index 1·336 and radius 7·8 mm. in which the pupil is imbedded at a distance 3·3 mm. from the "corneal" surface, the calculated apparent areas for various angles of view and for large and small pupils are shown in Fig. 3. The area for observation along the optic axis is taken as unity and allowance is made for a 5° separation of the optic and visual axes. The mean experimental curve for the large pupil is shown in the same diagram as well as the

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simple cosine curve which would be obtained if there were no corneal refraction. It is apparent that the calculated values deviate materially from the observed values for angles of view exceeding about 70°.

Good sets of pupil photographs at different angles are reproduced in Figs. 4 and 5. For these, the pupil has a non-zero and fairly well defined area at 105°, the largest angle used. In many cases the interpretation of the large angle photographs is difficult, particularly for brown (pigmented) eyes, where contrast between iris and pupil is low. In the example of Fig. 4 the far edge of the pupil approaches the corneal surface at 70° to 80° angle of view but subsequently recedes. Qualitatively, this is what would be expected from the simple theory mentioned above. There is considerable individual variation in the apparent position of the pupil at oblique angles of view.

If it is assumed that the apparent vertical diameter of the small pupil, like that of the large pupil, varies little with angle the average apparent area for pupils of any size and angle of view can be estimated approximately by interpolation. This is done in Table II, which assumes (1) that the relative apparent vertical diameters at different angles are the same for all pupil sizes and correspond to the values for the large pupil given in column 3 of Table I, (2) that, at a given angle, the ratio of horizontal to vertical diameters may be taken as a linear function of the apparent pupil diameter for normal view, *i.e.*, linear interpolation between columns 4 and 6 of Table II can be applied, (3) that the eye may be taken as a system symmetrical about an axis (the optic axis) inclined 5° to the temporal side of the visual axis.

Acknowledgment. The work described above was carried out in the Light Division of the National Physical Laboratory on behalf of the Chief of the Royal Naval Scientific Service, by whose permission this paper is published.

TABLE I

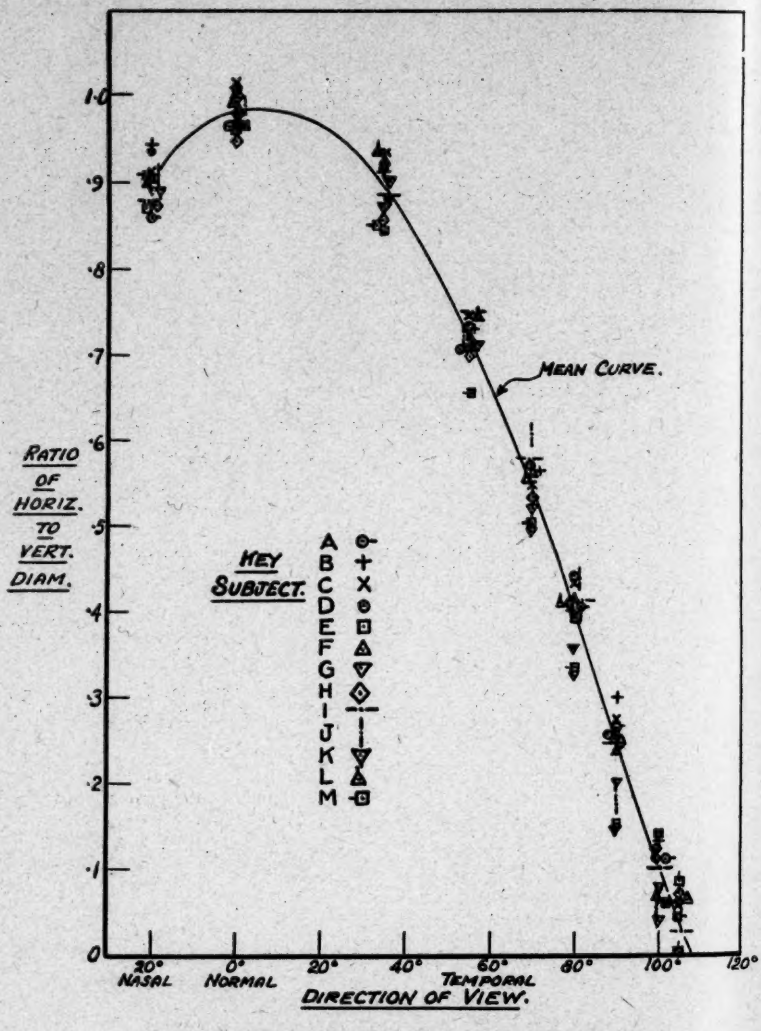
Direction of view of the camera with respect to the visual axis	Large pupil				Small pupil*
	Mean Appt. Hor. Diam.	Mean Appt. Vert. Diam.	Ratio of Hor./Vert. Diam.	Appt. Area	Ratio of Hor./Vert. Diam.
20° Nasal	7·13 mm.	7·94 mm.	0·90	44·4 mm.^{2}	0·91
0°	7·69	7·84	0·98	47·3	1·00
35° Temp.	7·01	7·83	0·90	43·1	0·90
55° Temp.	5·72	7·99	0·72	35·9	0·73
70° Temp.	4·43	8·15	0·54	28·3	0·53
80° Temp.	3·25	8·19	0·40	20·9	0·40
90° Temp.	1·18	8·15	0·23	12·0	0·28
100° Temp.	0·75	7·72	0·10	$4·5_3$	0·15
105° Temp.	0·25	7·44	0·03	$1·4_6$	0·07

* Mean apparent vertical diameter at 0° = 2·66 mm.

TABLE II

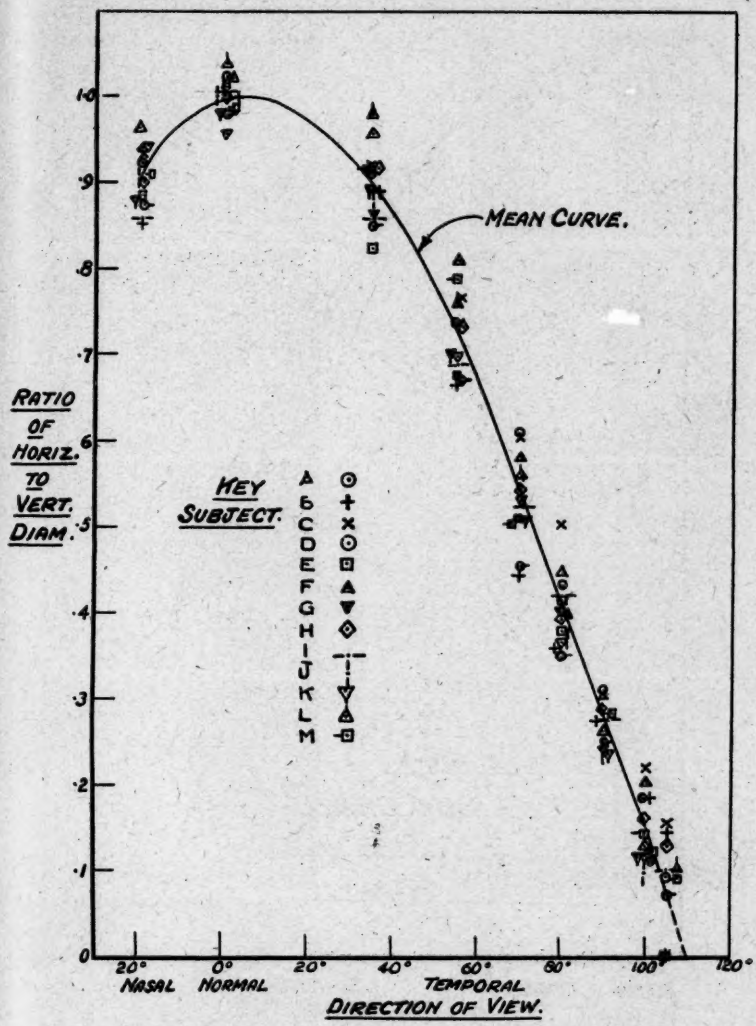
Factor by which the area of the apparent pupil is reduced for objects in the peripheral field. Area for an object on the visual axis taken as unity.

Angle between direction of object and the *optic* axis of the eye	Apparent pupil diam. for object on the visual axis			
	8 mm.	6	4	2
		Factor		
5° (corresponding for example to object on visual axis)	1·00	1·00	1·00	1·00
25	0·94	0·94	0·94	0·94
50	0·76	0·76	0·76	0·76
75	0·44	0·44	0·44	0·44
85	0·25	0·27	0·29	0·30
95	0·094	0·114	0·132	0·150
100	0·030	0·042	0·053	0·064



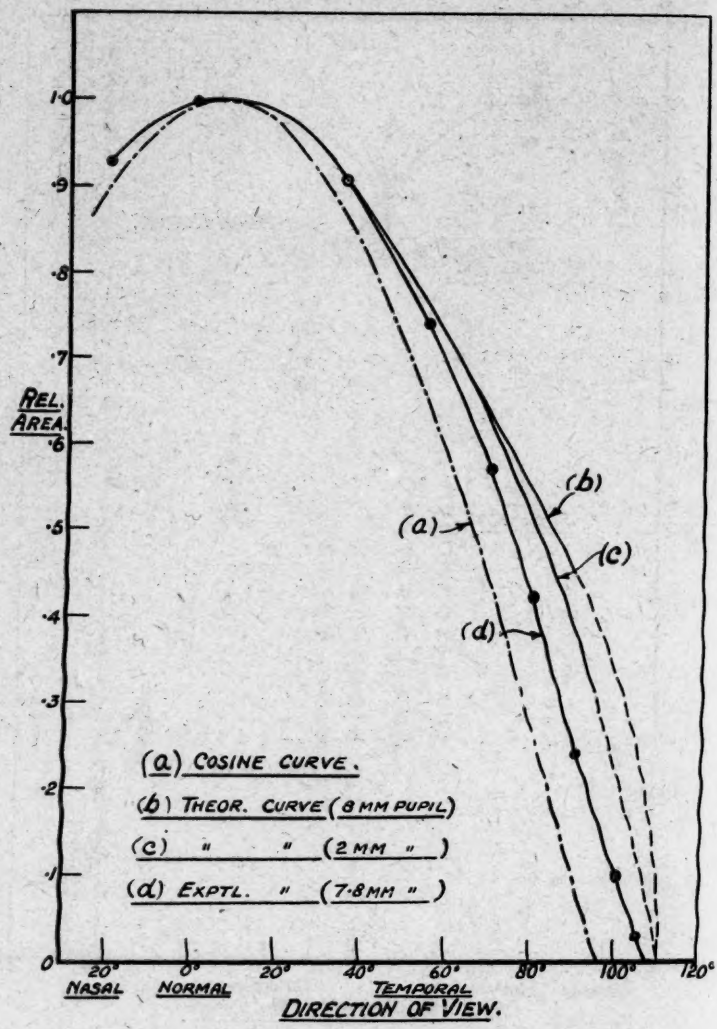
VARIATION OF PUPIL SHAPE WITH OBLIQUITY–LARGE PUPIL.

FIG. 1.



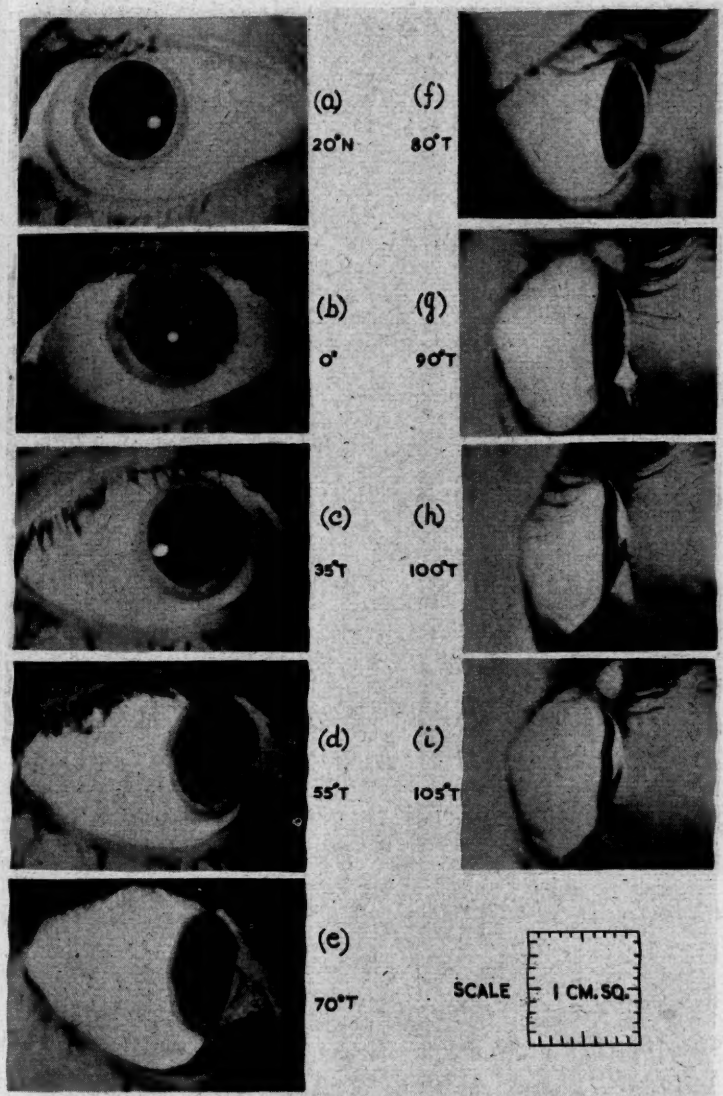
VARIATION OF PUPIL SHAPE WITH OBLIQUITY-SMALL PUPIL.

FIG. 2.



VARIATION OF RELATIVE PUPIL AREA WITH OBLIQUITY.

FIG. 3.



LARGE (DILATED) PUPIL VIEWED AT DIFFERENT OBLIQUITIES. SUBJECT "A".

FIG. 4.

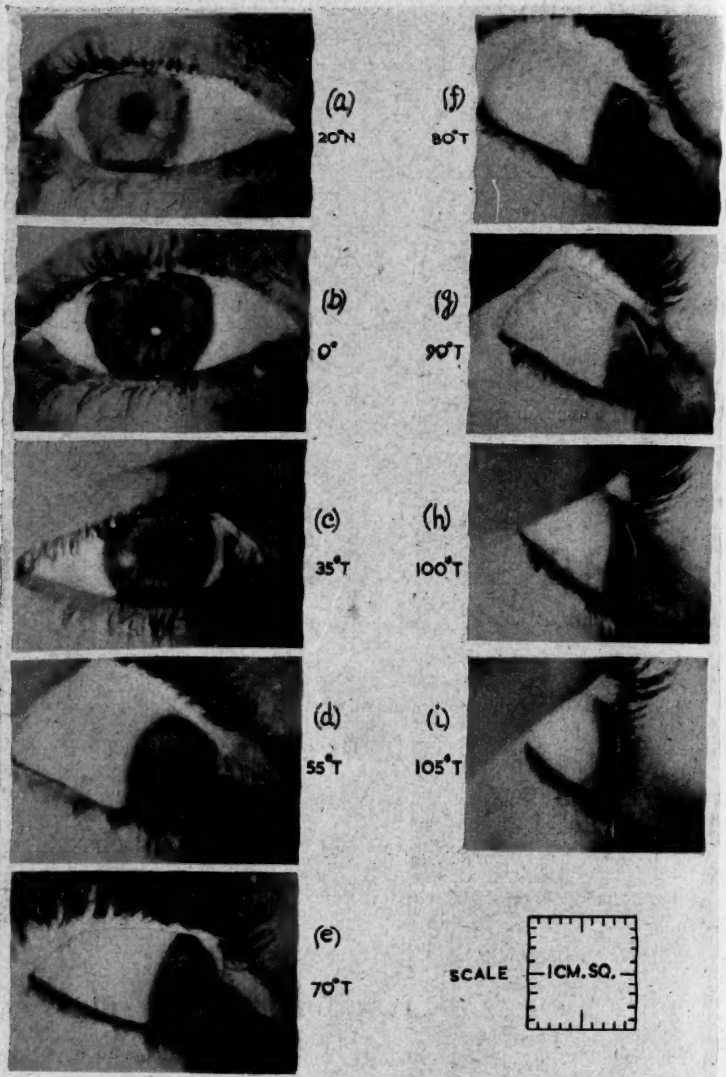

(a)
20°N
(b)
0°
(c)
35°T
(d)
55°T
(e)
70°T
(f)
80°T
(g)
90°T
(h)
100°T
(i)
105°T
SCALE
1CM.SQ.
SMALL PUPIL VIEWED AT DIFFERENT
OBLIQUITIES. SUBJECT "C."

FIG. 5.

THE ALTERATION IN SIZE OF THE NORMAL OPTIC DISC CUP *

BY

RANSOM PICKARD

EXETER

IN 1920 a paper (*a*) was read by me before the Ophthalmic Section of the Royal Society of Medicine in which it was deduced, from the sizes of the optic disc cups at different ages, that the cup normally increased in size with age. In another paper, read before the South Western Ophthalmological Society in 1935 (*b*) at Bath, a diagram was exhibited showing increases actually observed. In the present paper 234 eyes, observed for a period of fifteen years or nearly so will be compared with 280 eyes, observed contemporaneously with the fifteen year group, but observed only once, and not included in that group. Finally these two groups are combined together, and a general rule as to the average growth deduced.

All the discs recorded were normal in appearance. Cases of cataract were included if the discs were sufficiently clear to be drawn. Similarly small corneal nebulae were included. All other forms of disease in the eyes were excluded. There were no cases of abnormal congenital conditions in these series.

The method of recording was that devised by me in 1920 and practised by me since then. The outline of the disc is drawn of its apparent size. The outline of the cup at the surface of the disc is then drawn of its apparent size and in its proper position. Similarly the outline of the bottom of the cup is drawn. Usually the outlines of the surface and the bottom of the cup are connected by three or four lines. This last detail is unessential, but to my eye they serve to link up the two cup outlines together. Finally a note is made of the depth of the cup in dioptres. In the case of cups where the cup is larger at the base than on the surface, a bracket is made outside the disc margin at the place where this is so, and "bulbous" written there.

To estimate the size of the cup a transparent grid is used. The apparent size of the disc and of the cup surface are found, and the size of the cup expressed as a percentage of the disc.

The question of error in the estimate arises. No opportunity has occurred to compare my results with those of another observer on the same cases. It is estimated that there should not be more than five per cent. error in drawing the disc outlines, and two per cent. in measuring with the grid. This is sufficiently close for clinical purposes.

* Received for publication, November 8, 1947.

At the outset it must be pointed out that there are great variations from the average in the sizes, both at the first record and the subsequent occasions, in all age groups. This will be seen in the tables, where they vary from 5 to 100 per cent. And the possible variations are large. If the case of an initial cup varying from 5 to 50, and the final from 51 to 100 be considered the possible variations would be 2,250, which represents the maximum. And the number of eyes—234—multiplied into this will give an idea of the possibilities. Nevertheless, as happens in large collections, the actual cups cluster around the average.

Fifteen year group.—This consists of 234 eyes, observed for fifteen years or more, except for five, one of which was observed for fourteen years, and four between fourteen and fifteen years. For these extrapolation was employed, at the last observed rate of growth; it being thought that for so few cases and for so short a time, the total figures would not be vitiated.

TABLE I

Fifteen Year Groups

Age Groups	Number of Eyes	Average Initial Cups %	Initial Maxima	Initial Minima	Cups at 10 yrs.	Slope of Cups at 10 yrs	Slope of Cups at 15 yrs.	Total Slope at 15 yrs.
–10 yrs.	16	23	42	5	39	1·6	45	1·4
11–20 „	22	22	61	7	44	2·2	48	1·7
21–30 „	30	24	53	8	41	1·6	52	1·9
31–40 „	62	26	48	5	43	1·7	53	1·8
41–50 „	60	23	59	7	49	2·6	59	2·3
51–60 „	30	28	57	8	52	2·2	66	2·5
61–70 „	14	28	50	13	45	1·7	60	2·1
				Average Slope		1·9		1·9

Table I gives a summary of these eyes. The group clusters around early middle age, for about this time that the social circumstances tend to be more stabilised, and patients are more likely to persist in coming to the same oculist.

As will be seen later, the averages for the early years are rather

high, those for the later too low. The irregularity in the maximum initial cups should be noted; that for the 11-20 years is 61, the highest in the fifteen year group.

The slope is the percentage growth per year of the cups. It is an important measurement, for by this the rate of increase of the cups is ascertained, and the various cups compared with each other. Thus, the ten year group, derived from the fifteen year group by subtracting the growth of the last five years, is found by the slope to have the same value, 1·9, as the fifteen year group. This means that the average increase for the whole term is unaltered; although the individual cups differ from each other.

TABLE II

Alteration of slope (percentage increase of cups per year). Ten year group extracted from the fifteen year group.

Figures in brackets are the number of eyes in the various sub-groups.

Cup size sub-groups	Year Groups						
	-10	11-20	21-30	31-40	41-50	51-60	61-70
1-10 p.c.	2·9 (2)	3·2 (2)	2·9 (5)	2·5 (9)	3·8 (7)	4·6 (1)	—
11-20 „	1·5 (4)	2·9(12)	2·6(11)	2·5(15)	2·5(19)	2·4 (7)	2·5 (7)
21-30 „	1·7 (6)	1·4 (4)	1·0 (3)	1·5(26)	2·1(24)	2·3 (7)	0·0 (1)
31-40 „	0·7 (3)	1·5 (1)	0·9 (4)	1·5(10)	1·9 (6)	2·1(13)	0·6 (3)
41-50 „	1·7 (1)	0·2 (2)	1·3 (6)	0·6 (7)	0·6 (1)	1·1 (2)	1·4 (4)
51-60 „	—	—	0·6 (1)	—	0·0 (1)	—	—
61-70 „	—	0·3 (1)	—	—	—	—	—

An interesting condition is seen if the various age classes are separated out according to their cup sizes. In Table II this has been summarised in the slopes for the various values. With seven exceptions, the slopes have arranged themselves in such an order that the smaller initial cups have the higher slopes, the total number of the items being 37. Although some of the subgroups are quite small, the proportion of 30 to 7 is significant, all the more that the discrepancies, 0·2, 1·0, 0·1, 0·1, 0·4, 2·5 and 0·8, have among them three groups which each have only one eye.

This means that the smaller cups tend to catch up the larger, but they are only partially successful. The consistency of these cup

groups is surprising and was unexpected. The smallness of some of the groups, a statistical disadvantage, is counterbalanced by the occurrence of this inverse order in all the seven age groups.

TABLE III

Single Observations—Ten Year Groups—40 eyes in each group.

Year Groups	Average	Maxima	Minima	Slope
11–20	17	49	6	—
21–30	23	39	6	0·5
31–40	26	65	9	0·3
41–50	25	55	11	0·1
51–60	31	75	17	0·6
61–70	35	73	11	0·4
71–80	45	95	9	1·0

Single observations.—These consisted of 280 cups, in age groups of 40 each, seven groups in all, beginning at 11-20 years. They are displayed in Table III. The averages for the groups show a steady rise from the first to the last. The maxima are not so regular, but show a fairly consistent order; the minima are more irregular, they show that in some patients the cups remain small to the end. The slope cannot be stated, as only single observations were made on each case. If the order of the successive groups be taken as the increase per ten years, it will be seen that this agrees fairly well with the average found for the combined group. This single observation group is a better sample than the fifteen year group, for the number in each age group is the same for all ages; in the fifteen year eyes the smallness of the numbers in the early and the late groups decreases their usefulness statistically, unavoidable as this is.

Combined Group. With the object of smoothing out the irregularities in the two groups, both were combined together. The ten year groups, from the fifteen year groups, were taken instead of the latter, to conform more easily with the single observation group, which is arranged in ten year groups. From this mixture an average was found, which is used for the final deduction of the average course of

the disc growth. All the disc percentages thus obtained, their age groups being known, may be used, if they are kept in their proper age groups. The ten year cups will have to be included in the next batch to that from which they started. For instance, those derived from the 11-20 year group will have to be included in the 21-30 group for the purposes of this final estimate. Table IV shows the various averages as obtained from the separate groups, and the last set the average as obtained from their combination. (*See* Chart A).

TABLE IV

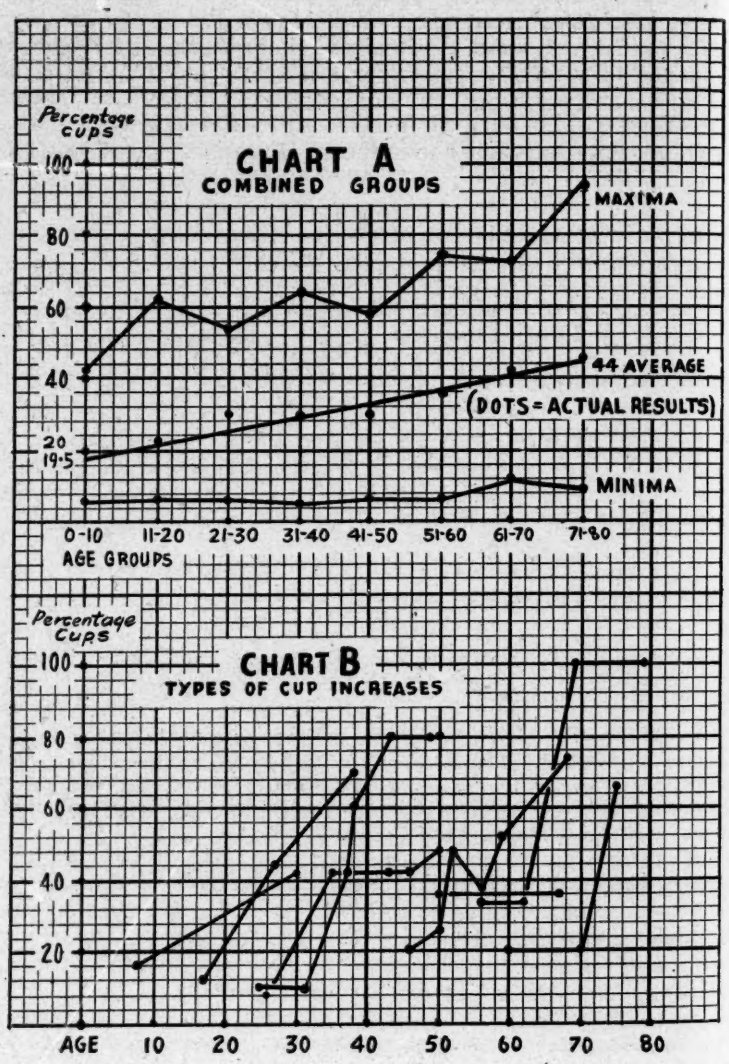
Average cups. Initial, ten year and single observations.

	No. of eyes	-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80
Single observations...	280	—	18	23	26	25	31	35	45
Fifteen year group									
Initial cups ...	234	23	22	24	26	23	28	28	—
Ten year cups ...	234	—	39	44	41	43	49	52	45
Combined average (Initial, 10 yr., and single observations)	—	—	23	29	29	31	36	41	45

Average slope. The chart A exhibits the final combined average for the various age groups, they are shown as black dots. They are nearly in a straight line. If a straight line is drawn from 23 (11-20 yrs.) at a slope of 0·35, it will cut the 71-80 yr. line at 44, and, if this is prolonged to the left, as far as the 0-10 column, it will cut it at 19·5. This is an average slope for the disc growth. The general formula is thus :— 19·5 + (0·35 × age in years) = Average cup for that particular year.

This formula must be taken for what it states, it is the average between the wide extremes of the maxima and the minima, as shown on Chart A. Nevertheless the nearly straight line shown by the actual figures shows that it is reliable as an average. The figures for the individual cases tend to group themselves around the averages, as should be the case if the latter are representative.

The practical point that follows is that any cup above 70 per cent. should be regarded as suspect, and be considered with the fields and tension before it can be said to be normal. It has seemed to me that a large cup cannot be accepted as physiological unless these precautions are taken.


Percentage cups
CHART A
COMBINED GROUPS
100
80
60
40
20
19·5
MAXIMA
44 AVERAGE
(DOTS = ACTUAL RESULTS)
MINIMA
0-10
11-20
21-30
31-40
41-50
51-60
61-70
71-80
AGE GROUPS
Percentage Cups
CHART B
TYPES OF CUP INCREASES
100
80
60
40
20
AGE
10
20
30
40
50
60
70
80

Decrease in the cups. In one eye the cup was 10 per cent. smaller at the end of fifteen years. Twelve others showed a decrease at some time, though all these were larger at the end of the fifteen years than at the beginning. These temporary losses were 3, 3, 4, 5, 5, 6, 6, 6, 7, 10, 10, and 10 per cent.

One cup was stationary for the whole period, it was 36 per cent. Five others showed very small increases 3, 3, 4, 5, and 6 per cent.

It is not uncommon to have a period of arrest of growth of the cup. This may occur at any period, when first seen, during the increase, or towards the end; examples are given in Chart B, which gives types of cup changes. It will be seen that in some of these the record extends over more than fifteen years.

Depth of the cups. Increase in depth tends to happen with the enlargement of the cup area, but irregularly so. It may be stated as a generalisation that if a cup enlarges to 60 per cent., its depth will increase generally by 0·5 to 1·0 dioptres, but by no means invariably so. A disc may increase to 100 per cent. and yet retain a depth of 1·0 D. An increase to 3 D, with an enlargement of the cup percentage must be investigated by the field and tension.

It is not easy to find any one cause for the cup enlargement. In the early years it can be attributed to the natural growth of the body, but this cannot be the reason for the continuous enlargement which goes on after youth, after the body has stopped growing. It may be other influences come into play which cause the enlargement to continue, which cannot be considered as pathological. Our bodies are always undergoing change, which in ordinary terms would not be thought abnormal, and are considered as part of the processes which lead to old age, yet are not, in general terms, thought to be pathological, though in an exact sense, they are. Perhaps the cup enlargement should be so considered. But this is merely to place it in a group of effects which we do not understand, though well recognised as the approach of old age. In the case of the eye, however, these changes do not affect the attributes of sight, according to the standards applied in the routine of ordinary practice, nor vision as used in every day life. It must be acknowledged that this is an analogy rather than an explanation.

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(*b*) *Trans. Ophthal. Soc. U.K.*, Vol. LV, 1935.

A PORTRAIT OF RICHARD BANISTER*

BY

ARNOLD SORSBY *and* W. J. BISHOP

LONDON

RICHARD BANISTER deserves well from English ophthalmology. As the editor of the second edition of the English translation of Jacques Guillemeau's *Des Maladies de l'Oeil qui sont en Nombre de Cent Treize aux quelles il est Subject*, and the author of the *Breviary* attached to this edition, he is the first English Ophthalmographer of note. The *Breviary* is a valuable document on the practice of the early ophthalmologist in this country, and is of outstanding historical importance because of an almost incidental passage which gives the first account of hardness of the eye as a diagnostic and prognostic sign. An unpublished manuscript by Richard Banister in the Sloane Collection at the British Museum, discovered by R. R. James, constitutes a further claim on posterity, for it is rich in detail on the social aspect of early English ophthalmology. These aspects of Banister's activities have been recorded fully elsewhere (Sorsby, 1932 (*a*) and (*b*); James, 1933; Sorsby, 1933; James and Sorsby, 1934).

James has established that Richard Banister died in 1626. The place and date of his birth are, however, still unknown. As he was admitted to the Company of Barber Surgeons in 1602 and the *Breviary* is dated 1621, when he writes of himself that "it is not long to the period of my daies," he may be assumed that he was at least between 40 and 50 in 1621. This would put his date of birth somewhere at around 1570-80.

A portrait at the Royal College of Surgeons is of interest in that it gives us a likeness of Richard Banister and a definite date of birth—if the authenticity of this picture can be established.

The portrait

History. The Minutes of the Royal College of Surgeons contain the following entry dated June 10, 1841.

> Mr. Stanley communicated at the request of Mr. Samuel Barton, of Manchester, a Member, that he Mr. Barton is in possession of an original Painting by Cornelius Jansen, in 1620, of Richard Banister, Author of Banister's Breviary; and that if it would be appreciated he would send it to be placed in the Library or Museum of the College.

* Received for Publication, April 17, 1948.

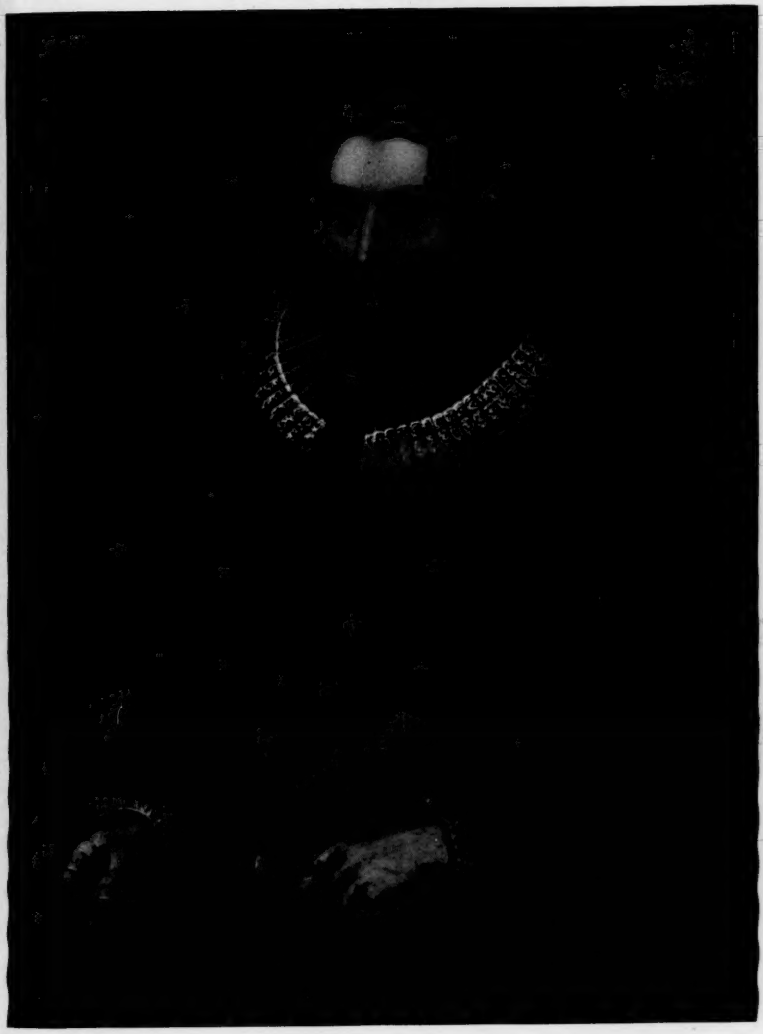

FIG. 1.

Photograph of a portrait of Richard Banister, Royal College of Surgeons.

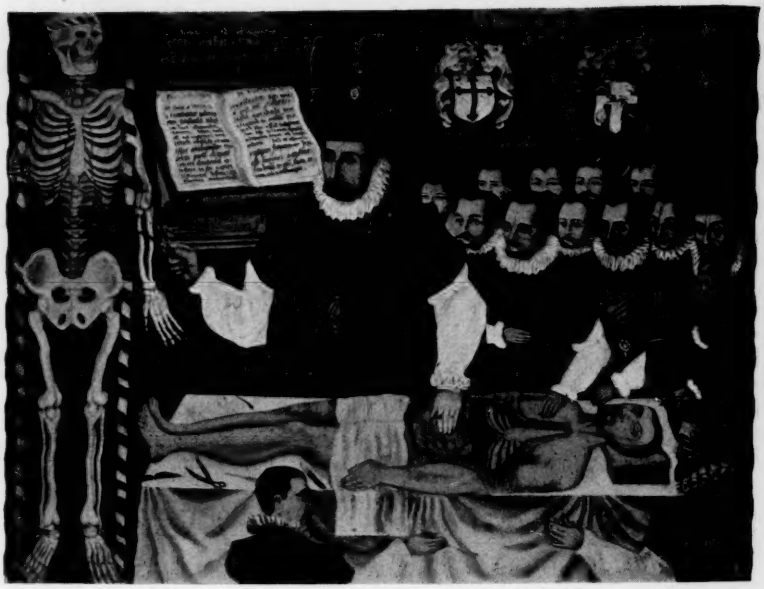

FIG. 2.

John Banister delivering the Visceral Lecture at the Barber-Surgeons' Hall in 1581. (From a contemporary painting now in the *Hunterian Library*, Glasgow. D'Arcy Power, 1913).

FIG. 3.

Photograph of the inscription in the top left-hand corner of the portrait of Richard Banister.

Resolved:

That Mr. Barton be informed that this Council are obliged by his liberal offer and will be much gratified by the possession of so interesting a Picture.

A month later, on July 8, the following Minute appears:

The Secretary laid before the Council for Mr. Barton of Manchester, the Portrait of Richard Banister mentioned to the Council by Mr. Stanley, at its last meeting.

Resolved:

That the best thanks of the Council be returned to Mr. Barton for such valuable Picture.

The portrait (Fig. 1) has a panel of 35 x 27 in. It has remained in the possession of the Royal College of Surgeons since 1841. In 1866 it was exhibited at the National Portrait Exhibition, when it was shown as a portrait of John Banister "a relative of Richard Banister," and ascribed to Cornelius Jansen. In Hallett's Catalogue of Portraits at the Royal College of Surgeons the portrait is given as that of Richard Banister painted by Van Ceulen; Banister's date of birth is given as 1585 and that of his death as 1633.

These dates and the ascription of the work to Van Ceulen are also given on the frame of the portrait hung in the hall of the College.

The Conflicting Data. It has been impossible to trace the history of the picture prior to its acceptance by the College in 1841. From the recorded data the picture might be either of Richard Banister or John Banister; and it would appear that its execution by Cornelius Johnson has not been questioned, for the different names mentioned all refer to the same significant contemporary of Van Dyck. None the less there is no reference to this picture in Finberg's extensive monograph on Cornelius Johnson. The available data therefore give no clear evidence as to the identity of the sitter or of the painter. There is in fact no evidence that it represents either Richard or John Banister.

The suggestion that the portrait represents John Banister can be clearly dismissed. There is a contemporary painting of John Banister in the Hunterian Library, Glasgow (Fig. 2) and this shows no facial (though possibly some family) resemblance to the sitter in this portrait. Moreover the picture carries the date of 1620 and gives the age of the sitter as fifty. Accepting these inscriptions on their face value John Banister must be ruled out for he was born in 1533 and died in 1610.

The possibility that the portrait does indeed represent Richard

Banister is not strengthened by what is known of his life. He was an itinerant oculist, and the highest civic distinction which he is known to have held was that of Churchwarden of Stamford. In his lifetime he was overshadowed by his famous uncle, and subsequently he became one of the forgotten figures of ophthalmology, though the fact that in 1841 Samuel Barton could regard the picture as of medical interest, and the Council of the College "were gratified by the possession of so interesting a Picture" suggests that his reputation was rather higher than present day memory would suggest. Still it remains an open question whether Richard Banister was of sufficient contemporary importance to have had a portrait executed—and that by an eminent painter.

Internal evidence from the portrait. These doubts are resolved by a study of the portrait itself, which brings out several things of importance:

(1) The inscription *Ats 50* in the top left-hand corner (Fig. 3) and of *1620* in the right-hand corner.

(2) The cross to the right of the inscription 1620.

(3) The box held in the sitter's left hand.

(4) The box at the side of his left hand.

(5) The instrument held in his right hand.

As for the two dates, authorities accept dates on portraits on their face value unless there is reason to doubt them. The fact that the shape of the ruff is that in fashion c. 1618-1632 (as Mr. C. K. Adams informs us) would justify accepting the validity of these inscriptions. Strong evidence that the sitter was a Banister comes from the cross in the right-hand corner. An illustration of this particular cross is given in Guillim's *A Display of Heraldry* (1638) under the designation of a cross flory. Edmonson's *A Complete Body of Heraldry* (1780) shows the arms of several branches of the Banister family; the arms of the Banisters of Leicester are given as a cross patonce, whilst those of another Banister without locality has the arms of a cross flory. The identification of the sitter as a Banister is further strengthened by the initials R.B. on the box at the side of the left hand, whilst the box held in that hand shows the first initial clearly, the second being covered by the hand. The possibility of the sitter being Richard Banister therefore becomes more tangible. If it could be proved that the instrument he holds in his right hand is a couching needle the evidence for the picture representing Richard Banister becomes fairly conclusive.

If the evidence for the identity of the sitter supports the traditional information on the picture, no such support can be obtained for the authenticity of the portrait as the work of Cornelius Johnson. On this technical issue we are obliged to Mr. C. K. Adams

for the following note, which he kindly prepared after studying the picture when it was removed from the frame and photographed.

" The portrait is a contemporary work having affinity to the work of native-born artists. It has been attributed to Cornelius Johnson. It is not, however, by such a skilled painter nor is the brushwork and colouring akin to his. It has suffered comparatively little at the hands of restorers and appears to be in all essentials, apart from the inscription, as originally painted.

The costume and type of ruff depicted are of between 1618 and 1632 and one might guess the sitter's age as being 45 or so. There is therefore no reason to question the date and age as inscribed on the portrait on these scores, though they have been very largely repainted. This is very apparent in the case of the A in " Aᵗˢ " where there are now visible three cross strokes to the A and two down strokes on the left hand side. " Originally there was apparently a diphthong 'Æ ' on a smaller scale than the more modern ' A.' The ' ts ' is of the same date as this alteration. There is room for the whole word ' Ætatis ' before ' 50 ' if written on the scale of the original ' Æ.' Part at least of the date 1620 is not the original paint as an old crack running down through the figure ' 2 ' has had to be made good on the surface to a width of half an inch. The ' 2 ' and half the ' 0 ' are certainly not original. Above the inscription ' Aᵗˢ 50 ' and about half an inch away from the top edge there is a mark which is highly suggestive of an inscription which has been almost entirely scraped away. Insufficient is left to read even a single letter. The appurtenances such as the instrument which the sitter holds, and the instrument boxes, and also the initials on the boxes appear to be contemporary with the original painting."

It may therefore be accepted that the portrait does indeed represent Richard Banister and it follows that the date of birth can be placed at 1570. This fits in with the indirect evidence previously available. To the appreciation that the Council of the Royal College of Surgeons expressed to Samuel Barton in 1841 for presenting the picture to the College, posterity may now add its own thanks for preserving this picture as a national treasure. Samuel Barton had a double interest in the portrait. He himself was one of the early surgeons to the Manchester [Royal] Eye Hospital, to which he was appointed in 1815. He died in 1871 after achieving local distinction as an ophthalmic surgeon, and as an enthusiastic collector of pictures and engravings.

We are indebted to the President and the Council of the Royal College of Surgeons for permission to study this portrait and for publishing this note; to the Secretary of the College for kindly

tracing the relevant Minutes, and Mr. S. Wood of the Library staff for information on Cornelius Johnson. To Mr. C. K. Adams, Assistant to the Director of the National Portrait Gallery, we are greatly obliged for the trouble he has taken, and for his ready guidance. We are also indebted to Mr. F. N. L. Poynter and Mr. C. A. Earnshaw of the Wellcome Historical Medical Museum for their interest and help. To Dr. O. M. Duthie and Dr. E. Bosdin Leech of Manchester we are obliged for their help in the fruitless search for the history of the portrait prior to its presentation to the Royal College of Surgeons.

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SOME NEW POINTS IN THE TECHNIQUE OF IMPLANT IN TENON'S CAPSULE AFTER ENUCLEATION

BY

ALBERT FAVORY

PARIS

IN some cases the implant of "acrylic" or any other material within the sclera after evisceration is not advisable, especially when sympathetic ophthalmia is threatening; enucleation is then absolutely necessary, and an implant in Tenon's capsule with fixation of the four recti can be done to obtain a moving prosthesis.

An implant within the sclera gives better movements to the prosthesis owing to the fact that the six ocular muscles are keeping their mobility even admitting that they are weakened more or less after the operation.

Among the numerous techniques described, Cutler's operation presented at the recent Oxford Congress appears as very seductive and exhibits very good functional results. Nevertheless, our personal

technique differs from Cutler's operation in many ways. The size and shape of the implant as well as the material used are not quite similar, so we shall emphasize these points of importance.

The fact that we should foresee a certain amount of shrinkage of Tenon's capsule after the operation led us to the opinion that the implant ought not to be too large; a ball of 10 mm. diameter is

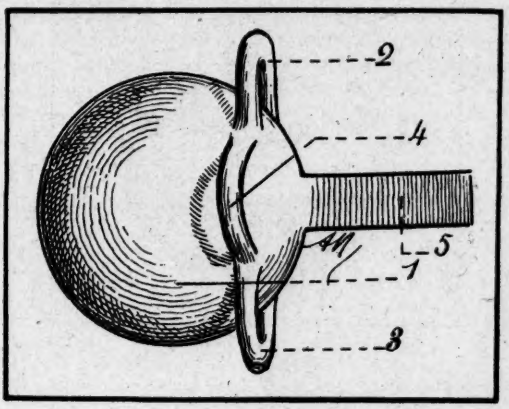


FIG. 1.

(After Virenque). Side view of implant. 1, body. 2, 3, 4, arches. 5, spur.

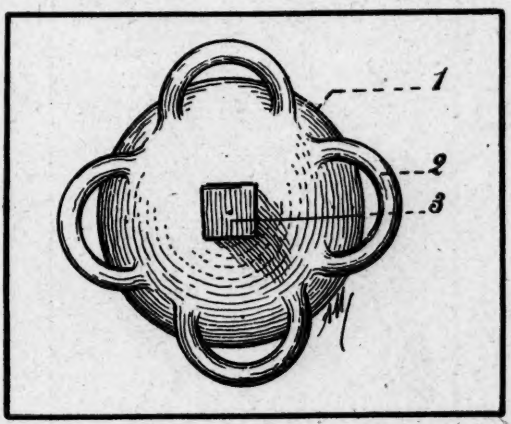


FIG. 2.

(After Virenque). Face view of implant. 1, body. 2, arch. 3, spur.

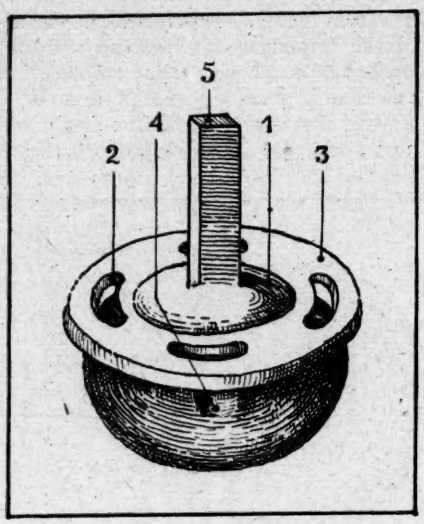


FIG. 3.

Face view of implant (new shape). 1, body. 2, oval-shaped hole. 3, disc. 4, groove. 5, spur.

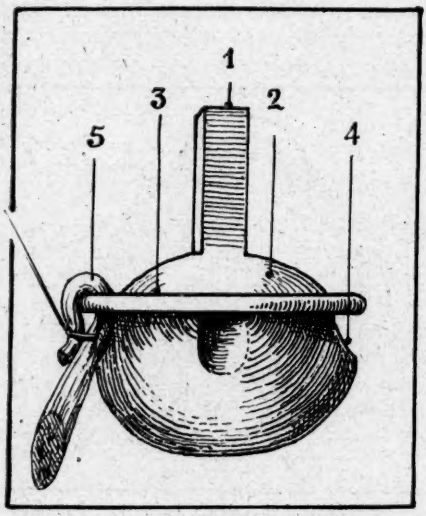


FIG. 4.

Side view of implant (new shape). 1, spur. 2, body. 3, disc. 4, groove. 5, muscle loop

sufficient, an excessive diameter may be the cause of its subsequent extrusion.

The only material used in our technique is "acrylic"; we think that the addition of a golden ring and pin makes the piece too heavy, and probably gold is not as well tolerated as acrylic, notwithstanding the fact that gold is a very rare material here in France.

Our implant is spherical in shape, its posterior surface being slightly flattened; four little arches of the same material as the ball are fixed near the anterior surface to receive the tendons of the recti. On the anterior aspect a spur of 15 mm. long and quadrangularly prismatic in shape is protruding (see Figs. 1 and 2. In a new shape the muscles are fixed on a disc with oval-shaped holes. On the implant body are four grooves to ease the muscle looping (Figs. 3 and 4). The operation is done with local anaesthesia, using a 2 per

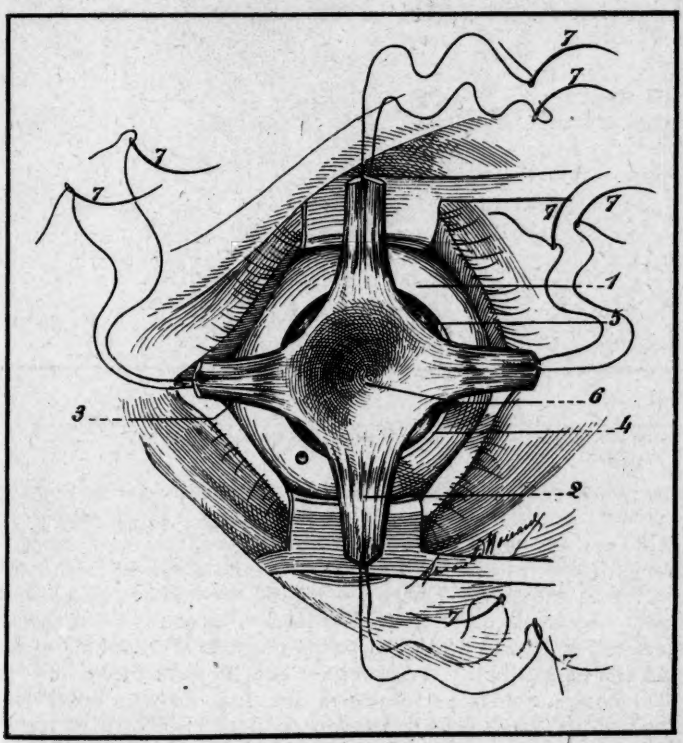


FIG. 5.

Enucleation complete (after Virenque). 1, 4 and 5, orbital tissue. 2 and 3, rectus muscle. 6, Tenon's capsule. 7, double armed silk stitch.

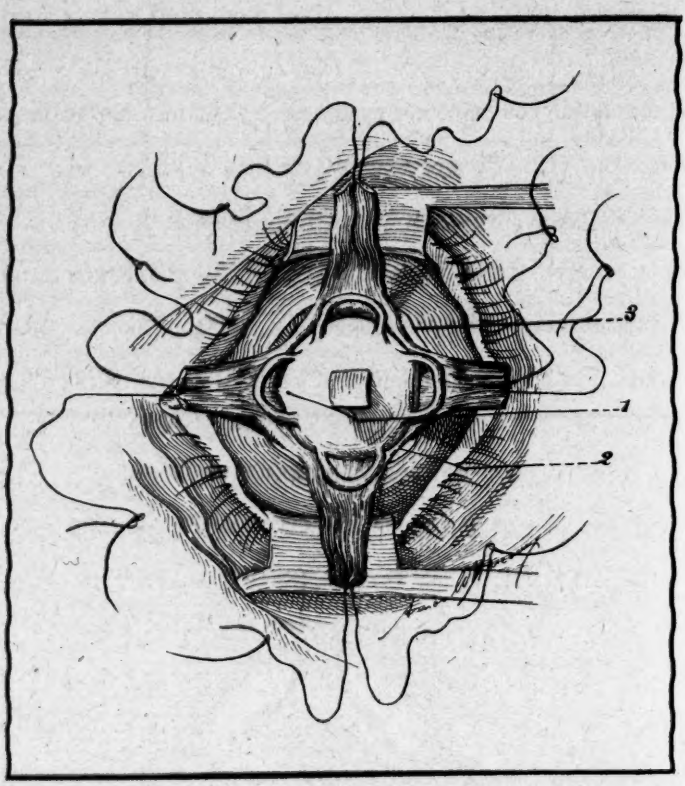


FIG. 6.

Implant placed in Tenon's space (after Virenque). 1, implant. 2, Tenon's capsule. 3, orbital tissue.

cent. solution of novocaine adrenalin for a retro-bulbar injection. *It is not necessary to add to this solution 1 c.c. of 40 per cent.* alcohol as is done in evisceration. The local anaesthesia is completed by *injecting a few drops of the same solution within* each rectus and subconjunctivally around the limbus. To keep the patient absolutely quiet, a *subcutaneous injection is done one hour* before the operation with nargenol (a mixture of morphia, scopolamine and ephedrine). We never use general anaesthesia.

The enucleation is performed in the usual manner, but a double armed silk suture is passed through the tendon of each rectus after this has been hooked. Then the eye is delivered, Tenon's capsule is inspected and haemostasis is carefully done with R.C. haemostatic (the main basis of this solution is extracted from pigeon muscle) (Fig. 5).

The implant is held in place in Tenon's capsule by grasping the spur with the forceps (Fig. 6).

The suture holding each rectus tendon is passed through each corresponding arch or hole, the tendon is then looped through round the arch or disc, the two needles of each suture being passed through the tendon and the silk passed through the conjunctiva and tied over (Fig. 7).

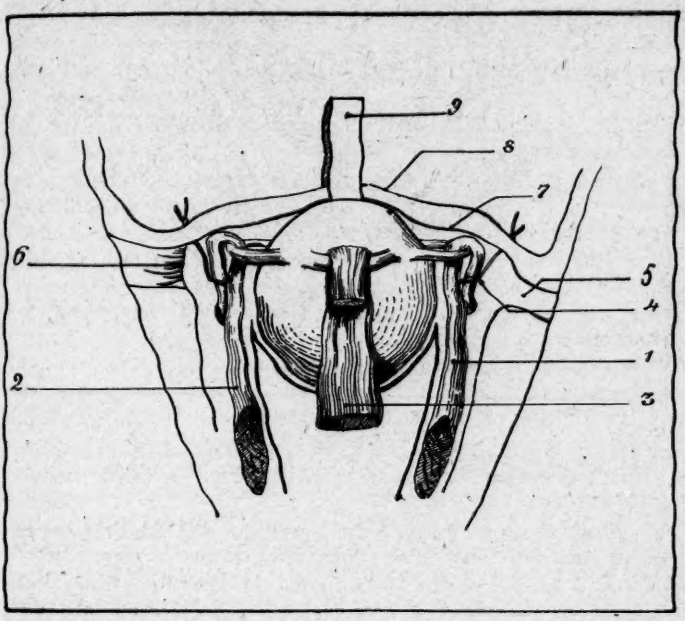


FIG. 7.

Semi-schematic cut of socket. 1, 2, 3, rectus muscle. 4, muscle stitch tied over conjunctiva. 5, Tenon's space. 6, socket space. 7 and 8; conjunctiva. 9, spur.

Tenon's capsule is sutured by separate catgut stitches and must be very carefully closed, conjunctiva is sutured over by five silk stitches each side of the spur (Fig. 8).

It seems that suturing the conjunctiva over the implant does not alter the deepness of the fornices owing to the conjunctiva's great elasticity.

At the end of the operation only the spur is protruding out of the conjunctiva and will later on enter a hole on the posterior surface of the prosthesis, A retainer shell is placed inside the lids to hold the implant and maintain the depths of the fornices.

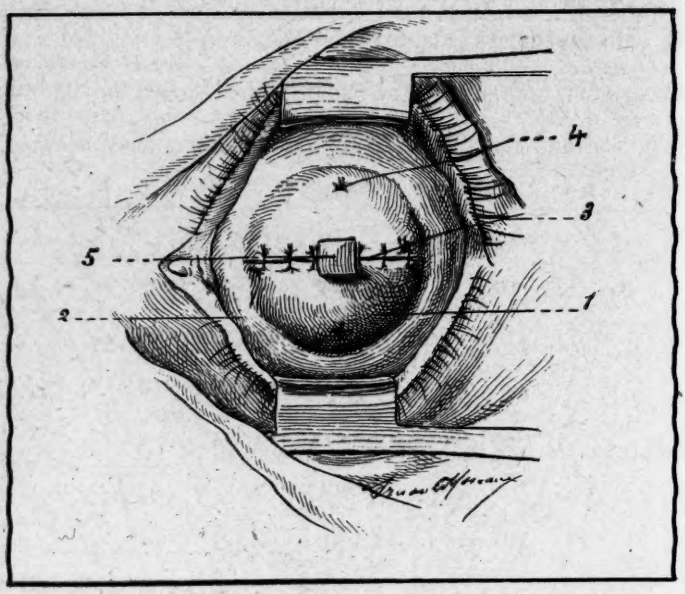


FIG. 8.

Completed operation (after Virenque). 1, implant covered by conjunctiva. 2, conjunctiva. 3, conjunctival suture. 4, rectus suture. 5, spur.

Very little reaction follows the operation and the dressing is not changed until after six days. The stitches are removed after ten days and a mould of the anterior aspect is done. The posterior surface of the prosthesis is made from the mould and will then fit perfectly well.

The shell is removed and the prosthesis is inserted as soon as possible, even if it is a provisional one to maintain the shape of the fornices. The final prosthesis may be adapted some weeks later. It is too soon to judge of the final value of this technique, as we have performed only a few operations.

We observed elimination of the implant in our first case. This was a bad case with an abnormal socket, and the piece used was too large. In another case the implant became prolapsed owing to the lack of firm suturing of the muscles. We had used catgut instead of silk to fix the muscles. In the other cases we were satisfied with the functional and cosmetic results.

We look forward to proceeding in this way and improving our technique by making any necessary modifications to ease its performance and to better its results.

ANNOTATIONS

The Passing of the Gratis Patient

When the writer started his practice the chink of the golden sovereign and silver shilling could still be heard in the land. Later, the rustle of the Treasury note superseded this comforting sound. In future it looks as if the only rustle to be heard in our consulting rooms will be that of the various certificates we shall have to complete. It is a solemn thought that after July 5, 1948, the gratis patient will have passed away. Some will perhaps say, with Mrs. Gamp, that it will make a lovely corpse; but our personal feeling will be one of regret.

Up to now a proportion of our work has always been on the free list; members of our own profession, their wives and families, the nursing sisterhood, curates and many of the poorer clergy, with those of small means whom we were asked to see by friends or patients. Provided we did not get too many gratis patients in any week we did not complain. You never knew what might turn up and even if it were nothing more exciting than a patch of opaque nerve fibres your time was not wasted.

A gratis patient and a grateful patient are not always synonymous terms, but very often they are, and among the writer's pleasant recollections are those of unsolicited thanks received from such people. Those of us who worked at Moorfields on Mondays and Thursdays in the early years of this century will recall how Sir Arnold Lawson's desk was usually piled high with bunches of flowers, a tribute alike to his professional ability and kindness of heart. We fear that in future these floral tributes will largely disappear along with much of the competition and friendly rivalry of the past. Emergencies in the streets will, we suppose, still be handled by the police and ambulance service. It would be highly improper were an apoplectic fit to be left in the gutter like a dead cat until his own medical attendant could be found.

The retired doctor is usually on the free list of some colleague. For the minor ills of life he can treat himself. Can he in future order himself ten grains of aspirin or will he have to attend a clinic and get a prescription? Should the writer get a mild conjunctivitis might he treat himself, or must he be "zoned," like fish, to the nearest ophthalmic surgeon? When that celebrated lawyer, Sir Edward Coke, was sent to the Tower by James the First he was told he might have legal assistance for his defence if he wished. His reply was—"I know myself to be accounted to have as much skill in the law as any man in England and therefore need no such help"; and, in the matter of a mild conjunctivitis, we must say we feel much the same. Perhaps, after all, as the undergraduate is

reputed to have written at the end of a Latin prose essay* : *hae autem observationes neque hic sunt neque illic.* But these remarks are neither here nor there. We merely throw them out for consideration, in placing this wreath upon the tomb of the gratis patient.

* Herbert Paul.—"Men and Letters."

Emotional Responses

It is an old saying that laughter and tears are near akin to each other. On the whole we think that in most people the risible element is more easily stimulated than the tearful, and perhaps also the more easily controlled. Pathetic passages in prose or verse may lead to weeping in some cases; parodies of the same will certainly lead to laughter and to tears only if one laughs too much.

Those who remember "Tom Brown's Schooldays" will recall George Arthur bursting into tears while construing a passage in the Iliad and the comments of his schoolfellows afterwards at his exhibition. In his case the stimulus would seem to have been partly visual and partly aural. Schoolboys as a rule are more likely to be risible than tearful; but we can remember an occasion in our own schooldays when the form was stumbling through the "Retreat from Syracuse" and making a hash of it. Suddenly the form master started to read us the Greek. The form was very nearly reduced to tears as a result. Speaking for oneself, one seemed to hear the wailing of lost souls as he was reading the passage. In this case the stimulus must have been an aural one, for most of us could have stared at the text all day without getting either the sense or any emotional response at all.

Belloc's Lord Lundy had the tearful response so well developed that he could not answer the simplest question without weeping, Ophthalmology at first sight does not seem to offer much scope for either response. But we must confess that there was an occasion on which we experienced a queer lacrymatory feeling long ago, when we were working through Fuchs' Lehrbuch, in order to try and teach ourselves to read German ophthalmology. It was in the account of the end results of amyloid degeneration of the conjunctiva. The English was a plain matter of fact statement: "Then is the eye lost." But the juxtaposition of "Augen" and "verloren" seemed more sonorous than the English equivalent and we suppose accounted for it.

A Scottish friend of ours once said that he could never read "Rab and his Friends" without tears. Many will agree with this instance.

The works of George Eliot abound in instances where the risible response is stimulated and in the "Scenes of Clerical Life" will be found examples where the tearful may come into play.

We do not think that our own pages ever stimulate a tearful response but there may be occasions where words have been misspelt or punctuation marks omitted when we provide the careful reader with a source for laughter.

In reading to oneself the brain not only sees the words, but must receive a kind of subconscious apprehension of what the passage will sound like if articulated in order to get the sense of the sentence. Visual, aural and mental processes must partake in some way to raise an emotional response of either kind. We confess that these waters are too deep for us to sail on, but some idea of what we intend is found in one of Charles Lamb's letters to Bernard Barton, the Quaker poet. "I can hardly read a book, for I miss the small soft voice which the idea of articulated words raises (almost imperceptibly to you) in a silent reader. I seem too deaf to see what I read. But with a touch or two of returning zephyr my head will melt."

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

THE 68th Annual Congress of the Ophthalmological Society of the United Kingdom was held on April 8, 9 and 10, at the Royal Society of Medicine, London. Over 200 members and many distinguished continental visitors, including the following, were present:—Professor Marc Amsler, Professor J. W. Nordenson, Professor H. Ehlers, Professor J. van der Hoeve, Dr. E. Pflueger, Professor E. Velter, Professor H. J. M. Weve, Professor A. Franceschetti, Professor Applemans, Professor W. H. Melanowski, Dr. H. Sjogren, Dr. T. L. Thomassen, Dr. A. C. Copper.

After a short opening speech by the President, Dr. A. J. Ballantyne, the topic for the morning's discussion, "Subjective Disorders of Vision (excluding those due to local ocular disease)," was introduced by Professor H. Cohen in a communication that was interesting, well-balanced, and beautifully delivered, followed by Dr. Denis Williams, who contributed also some original and important observations on the nature of "macular sparing" that showed an enviable mastery of the more recondite methods of perimetry; and by Mr. J. H. Doggart who continued ably and agreeably on this interesting subject. The discussion that followed could not maintain the high level of excellence that marked the opening speeches. A number of observations, interesting and sometimes entertaining, were offered.

The Bowman Lecture was delivered this year by Professor Marc Amsler. The subject chosen was "New Clinical Aspects of the Vegetative Eye," a clear and impressive thesis on the clinical and

scientific value of biochemical and biophysical micro-analysis of the aqueous fluid. These were beautifully illustrated by a film. Evidence was also given of the blood aqueous barrier, by the delay in appearance there of systemic fluorescein on slit-lamp microscopy, in chronic glaucoma, uveitis and systemic affections. The bearing of this in assessment of disease was illustrated.

The following papers were read during the Congress and covered a wide field :

" Ocular Palsies due to infection of the Nasal Sinuses " by Helen Dimsdale and D. G. Phillips ; emphasising with case histories the frequency of sinusitis as a cause of ophthalmoplegia, either coincidently by toxic effect, due to direct pressure of chronic sphenoiditis or due to periostitis of the superior orbital fissure.

" A Preliminary Survey of Forty-five Consecutive Cases of Congestive Glaucoma " by J. P. F. Lloyd ; concluding, *inter-alia*, that acute glaucoma does not often cause as acute symptoms as those classically described ; that those cases with gross visual loss may well have a thrombotic factor ; that recurrences are rare although gonioscopy shows obliteration of the angle of the anterior chamber after iridectomy ; stressing the inadvisability of using eserine after trephines, and the fundamental difference between acute and chronic glaucoma.

" The Conjunctival Naevus and the Neurogenic Theory of Melanomata " by Eugene Wolff ; discountenancing the neurogenic theory of their origin.

" Pictorial Demonstrations of Spasm of the Central Retinal Artery, Entoptic View of Retinal Vascularization, Hypophysial Tumour Causing Homonymous Hemianopia and III Nerve Paralysis, and Depigmentation of Iris in Chronic Glaucoma " by H. M. Traquair. In discussing these, E. Kraupa described how it was possible to see 2 or 3 vascular entoptic shadows, using 2 or 3 lights, and M. W. Paterson showed drawings of entoptic vessels that suggested a vascular raphe to the nasal side of the central avascular area.

" The Venous Pressure in Glaucomatous Eyes " by T. L. Thomassen. By ocular tonometry and manometry of the episcleral veins, venous pressure was shown to anticipate a rise or fall of intra-ocular pressure, the outflow of aqueous in aqueous veins being observed to be hampered as pressures are increasing and *vice versa*.

" Some Observations on Clinical Perimetry " by G. I. Scott.

" Cases of Subconjunctival Rupture of Globe by a Cow's Horn, and Arterio-venous Aneurysm " by G. T. W. Cashell, the former showing remarkable recovery of a disorganised eye with an avulsed iris, and contrasting with a case at the clinical demonstration of total iridectomy effected by a jackdaw. Two cases similar to the latter were demonstrated by A. Franceschetti.

"Papilloedema in Association with Toxic Hydrocephalus" by A. G. Cross. Follow-up of 32 cases showed only one case of optic atrophy and four of arcuate extension of the blind spot, and confirmed the inadvisability of early decompression.

"Latent Nystagmus" by T. Keith Lyle; six case histories of this condition in association with concomitant squint, emphasising the importance of binocular vision testing, and the undesirability of occlusion in such cases. A film was shown.

"The Classification of the Unassociated Dystrophies of the Fundus" by Professor Arnold Sorsby.

"Pictorial Demonstration of Pressure Grafting in the Contracted Socket with plunger anchored to a dental cap-splint, Epibulbar Dermoid, and Gummatous Ulceration of the Eyelids" by J. Ellison.

"Prognosis in Detachment of the Retina" by C. Dee Shapland, analysis of 155 cases.

"The Mode of Development of the Vascular System of the Retina with Some Observations on its Significance for Certain Retinal Diseases" by I. C. Michaelson. Retinal vessels originate by budding from other vessels, the capillaries from veins not arteries; hence in diabetes the veins and capillaries are principally affected, in hypertension, the arteries.

"Atropine in the Treatment of Glaucomatous Iridocyclitis" by Professor W. H. Melanowski. Six cases were discussed.

"Auto-Eversion of the Upper Lids" by W. C. Souter, film with anatomical discussion, an agreeably light note for the conclusion of the Congress.

A Joint Clinical Meeting was held in association with the Ophthalmological Section of the Royal Society of Medicine at the new Institute of Ophthalmology, and cases of interest were shown by Dr. Mary Cripps, Mr. A. G. Cross, Mr. A. C. L. Houlton, Mr. E. F. King, Mr. T. Keith Lyle, Mr. S. Philps, Mr. H. Ridley and Mr. P. Trevor-Roper.

A Trade Exhibition of ophthalmic instruments was also held during the Congress.

The Annual Dinner of the Society was held at the Royal College of Surgeons by kind invitation of the President and Council of the College. Professor Henry Cohen proposed the toast of the Society with polished urbanity, and the President replied. Mr. C. B. Goulden then welcomed the guests, who included Sir Alfred Webb-Johnson, Air Vice-Marshal P. C. Livingston, Sir Wilson Jameson, Sir Stewart Duke-Elder, Dr. A. F. MacCallan, Mr. F. A. Williamson-Noble, Professor Henry Cohen, Dr. Denis Williams, Mr. Frank W. Law, Mr. A. H. Levy, Mr. D. G. Phillips, Dr. Helen Dimsdale, and the foreign visitors already mentioned. Air Vice-Marshal P. C. Livingston, the Director-General of the R.A.F. Medical Service replied. Dr. H. M. Traquair toasted the President, and Sir Alfred Webb-Johnson closed the evening with an anecdote.

BOOK NOTICES

Diseases of the Eye. By SIR JOHN HERBERT PARSONS and SIR STEWART DUKE-ELDER. Pp. viii and 732. 21 plates. 368 text figures. London, J. and A. Churchill, 1948. Eleventh edition. Price 30/-.

It is in the nature of things that books relating to current medical practice tend to be almost ephemerides, not indeed creatures of a day, but equally not possessed of that diuturnity owned by some of the more philosophical of physicians' works. This must be so, for such books not only contain a foundation of basic and unchanging scientific fact, but must also be cognisant of that mass of new knowledge and theory which scientific research and clinical experience remorselessly accumulate; should they fail in this, they will inevitably be relegated to the dust and silence of the upper shelf to be superseded by the latest and most up-to-date work.

"Diseases of the Eye" is an old friend, not one of those who are never seen with new faces, yet one who, born again and again in the course of its forty-one years of life, retains its own essential character. In this process of palingenesis the book has contrived to keep abreast of developments as they occur with a balanced judgment and eclecticism which contribute no little to its value; new knowledge has not been included until its worth and importance have been proven, and new theories and methods of treatment have not been described simply because they are new.

To say that this edition of the work, under the joint authorship of Sir John Parsons and Sir Stewart Duke-Elder will be as welcome as have been in turn its ten predecessors, will be sufficient recommendation to the many of us who are already familiar with it. For those whose acquaintance with the literature of Ophthalmology is embryonic, one may say that as an introduction for students, general practitioners and junior ophthalmic surgeons, its value can hardly be exaggerated. With considerable economy of words it contains a mass of facts on anatomy, physiology, disease, treatment and the medical aspects of ophthalmology which will be of the greatest use to students and practitioners, and, when digested and illumined by clinical experience will advance the junior ophthalmic surgeon far along the path of his specialty.

The new edition closely follows the layout of its predecessors. More space is devoted, in view of their now proven value, to chemotherapeutic agents, although description of the well tried classical methods of treatment has not been omitted. The chapters on the neurology of vision and diseases of the nervous system have been revised, and diseases newly noted include epidemic keratoconjunctivitis, toxoplasmosis, brucellosis, and exophthalmic ophthalmoplegia;

certain recent advances in operative technique, such as Barkan's operation of Gonio-trabeculotomy are also mentioned. Altogether the book well fulfils its avowed object of being a safe, reliable and at the same time, modern introduction to diseases of the eye.

Handbook and Atlas of the Slit-Lamp Microscopy of the Living Eye. By ALFRED VOGT. Second Edition, Vol. III, Iris, Vitreous Body, Conjunctiva. 344 pages. 985 figs. (mostly in colour). 1948. Schweizer Bruck u. Verlagshaus, Zürich (H. K. Lewis, London). Price £16 10s. 0d.

As in all branches of human knowledge, so in medicine, great books are scarce and are to be treasured as fine gold. To this category belongs Alfred Vogt's Handbook and Atlas of the Slit-Lamp Microscopy of the Living Eye. As is now well-known, when Gullstrand first demonstrated the slit-lamp to the German Ophthalmological Society at Heidelberg in 1911, it is no exaggeration to say that a revolution was brought about in clinical ophthalmology. Since Gullstrand's early instrument was introduced a number of technical improvements have been made, not the least of which was the rearrangement of the illumination to provide brilliant and uniform optical sections of the tissues, a technique introduced by Vogt in 1920. Owing to its ease of access and the transparency of many of its tissues, the eye is thus available for examination in minute detail such as is attainable in no other part of the body; a microscopy of the living free from the mutilating technique of the morbid histologist is rendered possible, and the early signs of disease or the finer points of diagnostic or prognostic significance are determined in the eye with a certainty unobtainable in earlier days or in other organs to-day. The unflagging industry, sustained enthusiasm, and the brilliant and critical clinical acumen of Vogt, aided by a team of gifted colleagues in his clinic in Zürich and by unusually talented artistic assistance, made him the ideal exponent of the new method, and for a decade his clinic became the Mecca of ophthalmologists from the world over. From his clinic there poured a continuous stream of papers, many revolutionary in their observations, and these were collected and systematized in his "Atlas," the first edition of which appeared as a single relatively small volume in 1921. But as observation suceeded observation in greater and greater detail and time added significance to their value, a second edition of the book began to appear, the title changed from "Atlas" to "Lehrbuch und Atlas," and the size increased from one to three large volumes. The first, containing 692 illustrations with an abundant explanatory text on clinical methods, the cornea and anterior chamber, appeared in 1930; the second, bringing the number of illustrations up to 1507, is without doubt the most complete and authoritative treatise on the lens ever written; the third, bringing the number of illustrations up

to 2346, dealing with the iris, vitreous body and conjunctiva, is the volume under review. The first two volumes were written in German and published from Berlin: it is a sign of the times that the third is written in English and published from Zürich. The writing was completed in 1941 before Vogt's death, and the appearance of the book has been delayed for seven years.

In the space of a brief review it is impossible to give an adequate appreciation of this work, for it is unique in any branch of medicine. All the classical conditions are minutely described with abundance of case histories lavishly illustrated, and in addition there is a large number of new observations and new associations. Thus in connection with the pupillary border the efflorescences appearing in heterochromic iritis and the cysts arising from the long application of pilocarpine are described for the first time. The morphology of the pathological vitreous body takes on a new and unexpected interest as well as the part this structure may play in the formation of retinal holes in cases of detachment. Of great practical importance is the detail of the differential diagnosis which long-followed-up observations by the slit-lamp have rendered possible between simple and malignant pigmented tumours of the iris. A feature of the book is the stress laid upon genetics and hereditary conditions, one of Vogt's major interests. In this respect he has made a feature of the long-term study of the eyes of twins. His conclusions are of great interest, for example, that the microscopic details of the iris and their behaviour in extreme old age are pre-determined in the germplasm. Moreover, in a supplement to the study of the lens included in this volume, based on an imposing amount of evidence of the same nature whereby identical changes shared by monozygous twins are hereditary while variations are due to exogenous influences, he concludes that senile cataract is a phenomenon of ageing determined hereditarily on an exact parallel with greying of the hair or wrinkling of the skin. He follows out the interesting suggestion that the influence of medicaments on the formation of cataract can best be controlled by administering the medicament to one twin, the other being used as a control.

Vogt was a man of very decided views and with some of his theories it is reasonable to disagree; but he was one of the finest observers of this generation and no one can question his factual data. To anyone interested in ophthalmology or genetics this book will be found invaluable and indispensable; to the more general reader it is an object-lesson in scientific observation at its highest level enthusiastically applied and followed up. It is expensive to buy, but a book of this type is expensive to produce and in terms of value the price is cheap.

CORRESPONDENCE

BAILLIART'S DYNAMOMETER

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRS,—May I congratulate Mr. Foster on his valuable description of the continental clinics, but on one point only I disagree. I have used Bailliart's dynamometer for over fifteen years and I find this a reliable and important method in measuring the arterial tension in different branches of the vascular tree. The method is not easy, but once mastered is as precise as measuring of the blood pressure by a sphygmomanometer. I am usually satisfied with an approximate measurement without taking the intraocular pressure as well.

I am, Sir,
Your obedient Servant,

N. PINES.

41, PHILPOT STREET, E.1.
April 16, 1948.

OBITUARY

H. SECKER WALKER, F.R.C.S.

Ophthalmic Surgeon, The General Infirmary at Leeds.
April, 1863 — February, 1948.

BORN in 1863, the second son of Dr. Thomas Walker of Wakefield, Secker Walker was educated at the Grammar School of that city, and at University College Hospital, London.

Shortly after his appointment as Hon. Asst. Surgeon to the Eye, Ear, Nose and Throat Department of the General Infirmary at Leeds in 1890, he spent six months in Vienna, and after returning was one of the first Englishmen to perform a mastoidectomy.

From 1912, on the division of Ophthalmic and Aural Departments at the Infirmary, he confined his practice to ophthalmic surgery.

In 1914, H.H. The Jam Sahib of Nawanagar (the immortal Ranji) became his patient, after a serious grouse-shooting accident, and in gratitude for his recovery, in addition to naming a ward after Secker Walker in Nawanagar Hospital, "Ranji" provided the Leeds Infirmary with a new ophthalmic theatre, and out-patient department. The design of these incorporated many of Secker Walker's own ideas.

A keen Territorial from the founding of the force in 1908, he carried on the eye departments of the East Leeds and Beckett Park Military Hospitals from 1914-1918, being presented to His Late Majesty King George V at each of the Royal visits.

He was instrumental in persuading the authorities during this period to accept large numbers of men who had been rejected for defects that would be considered trifling in soldiers today.

Appointed Consulting Surgeon in 1919, he retired to the south, but kept up his professional activities, as a member of the Committee of the Bath Eye Infirmary, Pensions Secretary of the Wiltshire Association of the Blind, and as moving spirit and Chairman until 1939 of the Foundation Committee of the Bradford-on-Avon District Hospital.

His last public appearance was at the opening of this Hospital in September, 1947.

His manual dexterity both as an operator and as an amateur carpenter is a lively memory to such few of his colleagues as remain with us.

A more permanent memorial will be his influence on the design of the new Leeds Infirmary buildings, where his architectural ingenuity and untiring work are remembered with gratitude.

His publications include:—

Sarcoma of Iris. *Trans. Ophthal. Soc., U.K.* Vol. XV, p. 814. 1895.

Cysticercus of conjunctiva. *ibid.* Vol. XVI, p. 47. 1896.

Tumour of optic nerve. *ibid.* p. 139. 1896.

A diagrammatic model intended to assist in the teaching of ocular refraction. *ibid.* Vol. XXI, p. 142. 1901.

A model to illustrate the passage of rays of light through the eye in the various forms of astigmatism. *ibid.* Vol. XXV, p. 307. 1905.

Dr Luckhoff of Cape Town, writes:—

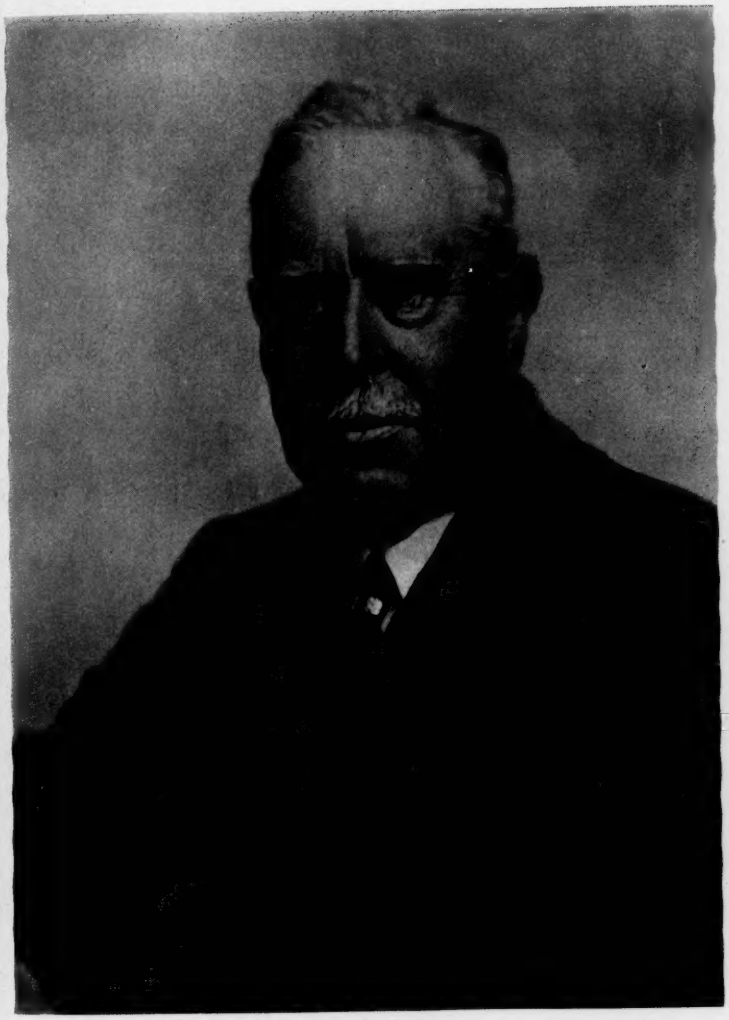
"..... How clearly I can visualise him, his springy alertness, his quickness of mind, his cheerful smile, and the quiet efficiency, equanimity, precision, and finish of everything he undertook.

His handwriting to the last showed the neatness, exactness, and good discipline of an orderly mind.

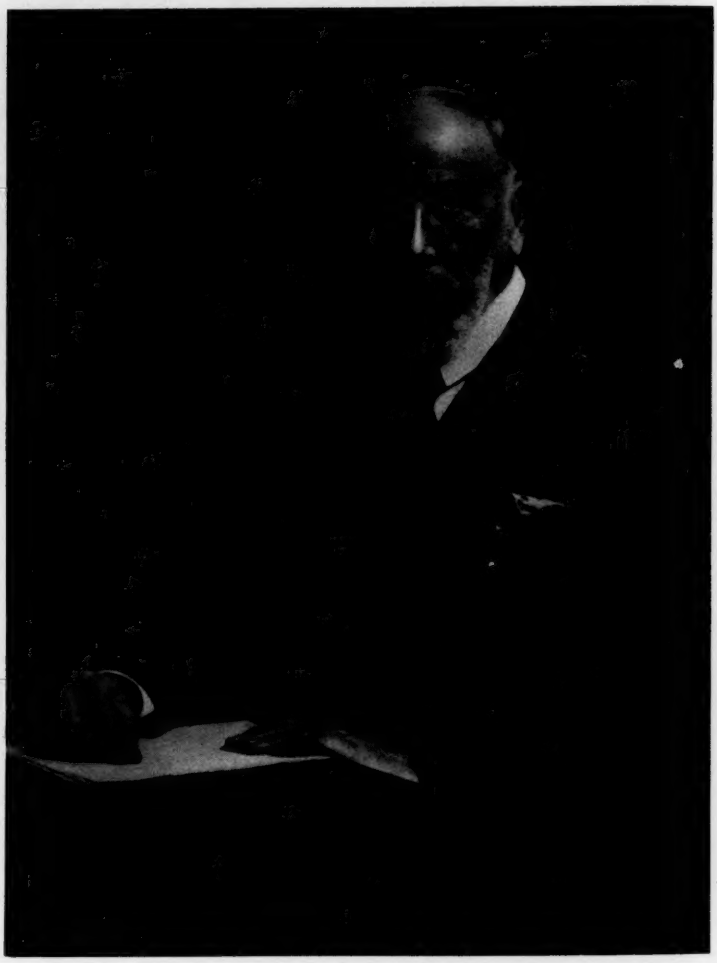
His complete integrity and openness of character was as refreshing as the nature he loved so well. I have no doubt that he was beloved and admired by all who knew him."

JOHN ROWAN

JOHN ROWAN died at his home near Prestwick on March 17. A native of Greenock, he retained his love and affection for the West of Scotland throughout his long life. He graduated M.B., C.M., in



H. SECKER WALKER



T. & R. Annan, Glasgow

JOHN ROWAN

the University of Glasgow in 1889, and received his early training in resident appointments in the Greenock Royal Infirmary. He was subsequently a clinical assistant at Moorfields and the Royal Westminster Ophthalmic Hospital. During these formative years, he made friendships which he retained steadfastly, and in his latter years he recalled with a quiet gusto the clinical incidents which had influenced his receptive mind. He made study visits to Berlin, Göttingen, Paris and Dublin, and returned to Glasgow in the early nineties. At that period, F. H. Napier, who now lives in retirement in Johannesburg, succeeded the celebrated J. R. Wolfe, known to several generations of medical students in relation to his method of skin grafting. Rowan became Assistant Surgeon to the Ophthalmic Institution, which had been founded by Wolfe in 1868, and retained this association throughout his life, being promoted Surgeon in 1916 and Honorary Consulting Surgeon in 1924.

He became a Member of the Ophthalmological Society of the United Kingdom in 1893, and was an original member of the Oxford Ophthalmological Congress. He was one of the pioneers of the ophthalmic examination of school children, and data from one of his early papers on the distribution of refractive errors in childhood were incorporated by Karl Pearson in his monograph on the inheritance of vision. Writing did not come easily to him, but he made several contributions to the proceedings of the various clinical and scientific bodies of which he was a member, and his remarks at meetings were frequently pawky and characteristic. In 1900 Rowan was elected a Fellow of the Royal Faculty of Physicians and Surgeons, and served on the board of management of the Glasgow Royal Mental Hospital and the Glasgow Veterinary College. At the meeting of the British Medical Association in 1922, he was vice-president of the Section of Ophthalmology.

He had a love for the country, and devoted much thought and care to the entertainment of his friends on a fishing or shooting expedition. About ten years ago, he retired from active practice, as he found that his progressive deafness was putting too great a strain upon his patients. Both his hospital and private work were carried out with meticulous attention to detail, and in the finest tradition of the great men whom he knew well in the old Moorfields. His manner could be aloof and distant, but once his confidence was gained, the discovery would be made that he was both shy and unassuming. He was for a long time associated with the Royal Sick Children's Hospital, and many old patients can recall his gentleness to them as children.

The present generation of ophthalmologists saw very little of him, and to some he represented the last of the Victorians. Ceremonial and formal they may have been, but we have lost the integration of

outlook and singleness of purpose which were strongly developed in John Rowan. He was a bachelor, and in the later years he would recall his old friends and teachers; for Nettleship and Treacher Collins he had unbounded admiration. He kept in touch by correspondence with old patients, friends and colleagues up to the end, and his interest in the progress of his chosen specialty did not fail.

NOTES

Honour

SIR STEWART DUKE-ELDER, K.C.V.O., and Mrs. Philippa P. Martin have been elected fellows of University College, London.

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Lectures

PROF. ARNOLD SORSBY will give two lectures on the dystrophies of the retina and choroid at the Royal College of Surgeons of England, on June 24-25, at 5 p.m. each day.

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Pan-American Association of Ophthalmology

DR. CONRAD BERENS has been elected President of the Pan-American Association of Ophthalmology. The next Congress is to be held in Mexico City in 1952. Twelve vice-presidents have also been elected. Dr. M. E. Alvaro was re-elected Secretary for Countries south of the Isthmus, and Dr. T. D. Allen succeeds Dr. Berens as Secretary for Countries North of the Isthmus of Panama. The Congress held in Havana in January of this year adopted statutes and by-laws, and permanent committees have been set up to deal with encouragement of research, glaucoma, trachoma, lighting and optics, contact lenses, orthoptics, prevention of blindness, neuro-ophthalmology, legal and industrial ophthalmology and other subjects.